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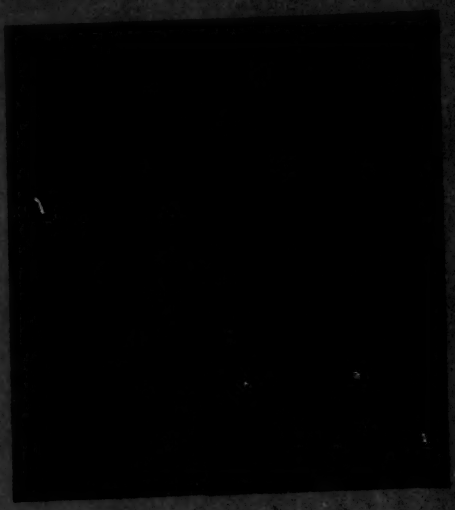

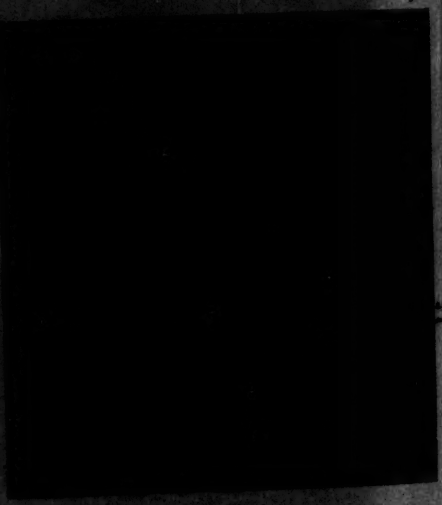

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COMMUNICATIONS

INVESTIGATIONS INTO HYALURONIC ACID AND HYALURONIDASE IN THE SUBRETINAL FLUID IN RETINAL DETACHMENT, PARTLY DUE TO RUPTURES AND PARTLY SECONDARY TO MALIGNANT CHOROIDAL MELANOMA

Preliminary Report Suggesting a New Hypothesis Concerning the Pathogenesis of Retinal Detachment*

BY

ERIK GODTFREDSEN

COPENHAGEN

INTRODUCTION

ALTHOUGH Meyer and Palmer isolated hyaluronic acid 15 years ago (1934), it was Chain and Duthie's discovery (1940) that the "spreading factor" is identical with hyaluronidase, the enzyme depolymerizing hyaluronic acid, which gave an impetus to the study of these biological substances. Hyaluronic acid constitutes

* Received for publication, July 21, 1949.

an important element of a number of the refracting media of the eye, and it is only natural that various valuable ophthalmological papers dealing with this substance should already have been published. Thus investigations have been made into hyaluronic acid in the cornea, the aqueous humour, the crystalline lens (Meyer 1938, 1940, and 1948), and the vitreous body (Pirie *et al.* 1948, Pirie 1949). But no investigations into hyaluronic acid in the subretinal fluid are available.

The object of the present investigation has been to test the subretinal fluid for hyaluronic acid as well as hyaluronidase for the purpose, if possible, of throwing some light on the numerous problems regarding retinal detachment. Demonstration of the presence or absence of these substances in the subretinal fluid may perhaps contribute to the elucidation of the pathogenesis of retinal detachment (the question of the share which the vitreous body has in the subretinal fluid), its diagnosis (serous detachment *versus* secondary detachment in malignant melanoma from the choroid, or in exudative retinopathy); and furthermore, its prognosis (chance of healing after surgical diathermy). Last, but not least, it may open new vistas for supplementary medication with antihistamines.

Before proceeding to the present investigations I shall briefly recapitulate the results of investigations by other writers, as well as modern views concerning:—

(1) the nature of the subretinal fluid; (2) the vitreous body; and (3) hyaluronic acid and hyaluronidase, with the main stress laid on conditions of importance for the following discussion. It is outside the scope of the present work to enter further on these subjects. Those interested may be referred to the comprehensive text-books (Duke-Elder) and the most recent articles in the journals (Meyer, Pirie).

THE SUBRETINAL FLUID IN RETINAL DETACHMENT

This fluid has been analyzed for a great number of physical as well as chemical properties, most recently and most thoroughly by Weve and Fischer (1937, 1939, and 1940), while hyaluronic acid and hyaluronidase investigations have not so far been reported.

The pathogenesis of the subretinal fluid is not quite clear. Most writers (Weve and Fischer) hold that the subretinal fluid consists mainly of vitreous body penetrating subretinally *via* the retinal rupture. This genesis is, however, denied by Magitot (1934). Koyanagi (1934) supposes the subretinal fluid to be secreted from the pigmentary epithelium of the retina. This

harmonizes with the theory that the main site of production of normal vitreous body is the pigmentary epithelium.

The passage of vitreous body *via* the retinal rupture is easily envisaged in cases displaying large ruptures at the ora, but these are rare. In detachment after small or even minimal ruptures it is more difficult to understand how vitreous body could penetrate, though indeed liquefaction of the latter may totally change the possibilities of transfer (see later).

If a retinal rupture is demonstrable—and careful examiners can nearly always find one—the subretinal fluid is relatively clear, yellowish, mucous and ropy, and it does not coagulate on standing. Where the detachment is of longer duration the albumin content will increase, possibly under the influence of transudation from the vessels of the choroid. In cases of very long-standing detachment the albumin may altogether disappear simultaneously with atrophy of the choroid (Duke-Elder). The part of the vitreous body which penetrates subretinally will undergo certain successive changes and become admixed with heavy water and protein from the choroid (Weve and Fischer 1940).

If the retinal rupture is *not* demonstrable (in these cases it is hardly a question of primary serous detachment, but rather of exudative retinopathy—whether locally induced or of systemic origin), then the subretinal fluid is highly coagulable, jelly-like, grey and albuminous, often with admixture of blood. This finding is analogous to inflammatory exudates in other parts of the organism.

In cases of malignant melanoma of the choroid the subretinal fluid is highly albuminous. The albumin yields the special yellowish colour visible on ophthalmoscopy (Ronne 1936). Adequate physico-chemical analyses of the subretinal fluid are missing in these cases.

In serous detachments analyses of the subretinal fluid have revealed great variations in the albumin concentration (about 135 - 60 per cent.), sugar values as in the vitreous body, and a chloride concentration differing from that of blood plasma (Duke-Elder). Jasiniki has made viscosity tests (1933). The following enzymes have been demonstrated: amylase (Weve and Fischer 1937) and acetyl-cholinesterase (Weve and Fischer 1939).

THE VITREOUS BODY

The vitreous is not, as previously believed, of a cellular nature, but a gel comparable to a mass of plasma (Davson 1949). If the water is evaporated " residual protein " will remain, together with the polysaccharide hyaluronic acid—the latter being a

protein-free substance erroneously called mucoprotein in the past. These two non-haematogenous substances determine the special structure of the vitreous body (Pirie 1948 and 1949), in which the high viscosity is due to hyaluronic acid. The hyaluronic acid is responsible for 30 per cent. of the organic weight of the vitreous body (Meyer 1948).

Recent comprehensive analyses made on frozen sections of vitreous body showed in several respects a chemical resemblance to the aqueous humour (Duke-Elder and Davson 1949), but there was a great difference with regard to phosphate content (Palm 1948).

The vitreous body has been demonstrated to contain the following enzymes: amylase, proteinase, and acetyl-cholinesterase (Uvnäs and Wolff 1938). The action of these enzymes is accelerated by change of pH in the acid direction, and an autolysis may take place. Liquefaction of the vitreous body may also occur through haematogenous enzymes, notably hyaluronidase, which (see below) specifically depolymerizes the hyaluronic acid into low-molecular reducing agents.

HYALURONIC ACID AND HYALURONIDASE

Hyaluronic acid (Meyer and Palmer 1934) is present in the ground substance of connective tissue, the jelly of Wharton in the human umbilical cord, the synovia of joints, and abundantly in the vitreous. Smaller amounts exist in the cornea, aqueous and crystalline lens, but not in blood and cerebrospinal fluid. Chemically hyaluronic acid resembles the anticoagulant heparin. It is a high-molecular polysaccharide, a polymer of a disaccharide consisting of glucuronic acid and N-acetyl glucosamine (a hexosamine). The molecular weight has not been finally settled. It depends on the degree of polymerisation, but is within the range of 200,000 to 500,000. The hyaluronic acid, probably produced from the cells of the connective tissue (type not yet elucidated), presents as a mucous, highly viscid fluid. The high viscosity conditions the resistance of connective tissue (and other tissues) to passage of both corpuscular elements (bacteria, Indian ink particles) and liquefied substances (toxins, snake venom, etc.).

The enzymatic depolymerisation of the hyaluronic acid is due to the specific enzyme hyaluronidase (Chain and Duthie 1940), which is identical with the "spreading factor" previously demonstrated in extracts of testis, malignant tumours, snake venoms and bacterial cultures (Hofman and Duran-Reynals 1930, McClean 1930). Hyaluronidase is prepared from bull semen and is a high-molecular substance, which has not yet been produced in pure form. Addition of hyaluronidase to a viscid hyaluronic

acid solution will cause a prompt depolymerisation of the hyaluronic acid into glucuronic acid and glucosamine, and the fluid will now become thin like water. The depolymerisation of the high-molecular hyaluronic acid into the low-molecular reducing disaccharides may in part be followed viscosimetrically, and partly by the power of reduction.

The sites of production of hyaluronidase are, in cases of infection, the bacterial elements, and, in cases of malignant tumours, presumably the supporting elements of the tumour tissue. Mayer and Kull (1947) have shown that an allergic tissue reaction, *e.g.*, within a skin area, will involve local production of hyaluronidase, which, by its influence on the hyaluronic acid of the connective tissue, contributes to the allergic process—in this instance spreading of oedema. Mayer and Kull succeeded in inhibiting the hyaluronidase activity by antihistamines (pyribenzamine). This opens new prospects for our understanding of the allergic process and the possibility of supplementary therapy.

A quantitative estimation of hyaluronic acid is still difficult. Such is based partly on viscosimetry (Meyer; Dalgaard-Mikkelsen and Kvorning), and partly on reduction determination of the reducing depolymerisation products. The relation of viscosity to quantity is not yet elucidated. Hyaluronidase is estimated biologically by its effect on the hyaluronic acid, partly *in vitro* (viscosimetry) and partly *in vivo* by the rate of spreading of Indian ink particles injected subcutaneously.

PRESENT INVESTIGATIONS

The series on which the present investigations are based comprises 17 patients with retinal detachment, whose data appear from Table 1. Some of the patients were admitted to the Kommunehospital and some to the Rigshospital, Copenhagen. There were 9 females and 8 males ranging in age from 16 to 65 years. *The retinal detachment* had the following *causes*: direct trauma in five cases (1, 2, 3, 4, 5), excessive myopia in five cases (6, 7, 8, 9, 10), uncertain or unknown cause in another five cases (11, 12, 13, 14, 15), of which, however, case 15 presented a generalized exudative disease: Besnier's prurigo with simultaneous syndermatotic cataract. In two cases (16, 17) the retinal detachment was secondary to a histologically verified malignant choroidal melanoma.

The extent of the retinal detachment is indicated in retinal squares, from one-fourth to four-fourths with the following distribution: two cases one-fourth (9, 13), seven cases two-fourths (1, 3, 5, 8, 11, 12, 16), three cases three-fourths (6, 7, 10), and finally five cases total detachment (2, 4, 14, 15, 17); thus a representative series.

TABLE I—The relative viscosity of the subretinal fluid in 17 cases of retinal detachment

Case No.	Sex Age	Retinal detachment: Etiology	Size in squares	Tear	Duration in mths	The subretinal fluid: Relative viscosity	Hyaluronidase	Comments
1	F.-25	Traumatic	2 4	?	12	1·30	—	
2	M.-39	—	4/4	+	1	1·30	—	
3	M.-51	—	2/4	+	1	1·20	—	
4	F.-46	—	4/4	+	1½	1·50	—	
5	M.-49	—	2/4	+	1/10	1·00	—	1940 I detachment Now 1949 re-operation
6	M.-46	Excessive yopia	3/4	?	2	1·30	—	
7	F.-43	—	3/4	+	1	1) 1·40 2) 1·10	— —	1) from the bulk + tear 2) from the bulk — tear
8	F.-54	—	2/4	+	1/10	1·20	—	
9	F.-44	—	1/4	+	1/2	1·10	—	
10	M.-29	—	3 4	+	1	1·10	—	Total detachment in the other eye previously
11	F.-23	questionable	2/4	—	?	1·30	—	
12	F.-65	?	2/4	+	1	1·30	—	
13	F.-62	?	1/4	+	3	1·30	—	
14	F.-50	?	4/4	+	18	1·10	—	Case of re-operation
15	M.-16	Besnier's Prurigo	4/4	—	?	1·0	—	Generalized exudative diathesis affecting the skin, etc., + cataract syndermatotica. Re-operation.
16	M.-50	Melanoma malignum choroid	2/4	—	1	1·0	—	
17	M.-35	—	4/4	—	8	1·0	—	

Retinal rupture was definitely found in thirteen cases, and suspected in two others. Rupture was not observed in four cases, of which two with melanoma and two of an exudative character (cases 1 and 15), the latter the one with Besnier's prurigo. The ruptures were in all cases rather small. Some were of the ordinary horse-shoe type, while others were of the cribriform, cystoid type. None of the cases presented disinsertion or large rupture at the ora serrata.

The *durations of the retinal detachments* were as follows: less than one month in three cases (5, 8, 9), one to three months in nine cases (2, 3, 4, 6, 7, 10, 12, 13, 16), and from three to eighteen months in three cases (1, 14, 17). In two cases the duration could

not be fixed (11, 15). The retinal detachment was treated by ordinary surgical diathermy (according to Larsson-Weve), except in the two cases with malignant melanoma, where enucleation was performed. Course and result will not be discussed here. During the operations the subretinal fluid flowing through the scleral perforations was collected and placed in a refrigerator. Possible admixture of larger or smaller amounts of blood proved to play no great part for the further investigation, since blood contains no hyaluronic acid.

The subretinal fluid was then tested as soon as possible for hyaluronic acid and hyaluronidase in the Department of Pharmacology, University of Copenhagen. These tests were performed by the *viscosimetric technique* recently elaborated by Dalgaard-Mikkelsen and Kvorning (1948). Although the method, the details of which appear in the original article, is a sensitive micromethod, a dilution of 1 in 10 of the subretinal fluid was chosen in the majority of the cases, in order to obtain a sufficiency of material for examination. The procedure consisted of placing the diluted, subretinal fluid in the specially constructed viscosimeter, where, at a constant temperature, the duration of flow through a capillary tube with a given lumen was measured in seconds. Three or four control measurements were made. The flow-time for distilled water is 80 seconds, but for diluted subretinal fluid flow-times up to 120 seconds have been noted. In the cases where the flow-times exceeded that for distilled water a little hyaluronidase was added to the solution, and then, after a few minutes' standing, another series of readings was taken. This brought about prompt reduction in the flow-time, *e.g.*, from 120 to 90 seconds. The relative viscosity was calculated on this basis, and the values have been set out in Table 1.

The changes observed in the flow-times after addition of hyaluronidase can be due only to the fact that the previously viscid solution has changed its character in consequence of the depolymerisation of the hyaluronic acid. If the genuine, subretinal fluid presented flow-times approximately corresponding to that for distilled water, so that we may exclude the presence of hyaluronic acid, the solution was *tested for hyaluronidase* content by addition of a known standard solution with hyaluronic acid.

In a small number of cases there was occasion to determine the relative viscosity of both undiluted and diluted (1 :10) subretinal fluid. To give an idea of the reduction of the relative viscosity brought about by dilution it may be stated that relative viscosity 1·3 in dilution 1 :10 corresponds to relative viscosity 4·0 in undiluted fluid. As, however, the present investigation aims only at a preliminary qualitative estimation, these facts will not be

discussed further. They will be dealt with in greater detail in future papers.

The *relative viscosities in the subretinal fluid* were as follows:

In the five cases of traumatic origin: 1·20-1·50 in four cases, and 1·0 in one case (5) (re-operated on).

In the five cases with excessive myopia: 1·10-1·40. In one case (7) the value was much higher in a sample from the site of rupture (1·40) than in one from another part, where no rupture was found (1·10).

In the five aetiologically uncertain cases: 1·30 in three, 1·10 in one (14) of re-operation, and 1·0 in one (15) presenting Besnier's prurigo.

In the two cases of malignant choroidal melanoma: 1·0.

Since relative values of 1·10 or more are suggestive of the presence of hyaluronic acid, it appears that *hyaluronic acid was found in all the cases of serous detachment,* except two submitted to re-operation (5 and 14), and one of exudative retinopathy as part of a generalized exudative disease (Besnier's prurigo). Hyaluronic acid was *absent in both cases of malignant choroidal melanoma.*

Hyaluronidase was demonstrable *in none* of the 17 cases.

Regarding the relation of the duration of the retinal detachment to the amount of hyaluronic acid, estimated approximately on the basis of the relative viscosity, it appeared that the highest relative viscosities—and thus the highest hyaluronic acid values—were found in the cases of 1 to 3 months' duration. The cases of shorter and those of longer duration, on the other hand, presented lower relative viscosities, such comparatively small material must be cautiously interpreted.

There appears to be a definite correlation between retinal *rupture and relative viscosity,* since hyaluronic acid was present in all cases of rupture, except those re-operated on owing to recurrence, where special conditions asserted themselves.

DISCUSSION

Although the present investigation is based on a rather small number of cases of retinal detachment, the results of the hyaluronic acid analyses in the subretinal fluid are fairly uniform. It appears that in primary, serous, retinal detachment the subretinal fluid contains considerable amounts of hyaluronic acid, which are responsible for the characteristic ropy and mucous character of the fluid. In cases of malignant choroidal melanoma with secondary retinal detachment, on the other hand, the subretinal fluid is not viscid, and hyaluronic acid could not be demonstrated. In two cases of recurrent detachment and one of

exudative retinopathy as part of a generalized disease (Besnier's prurigo) no hyaluronic acid was found.

The fact that such large amounts of hyaluronic acid were demonstrated in all the cases of primary serous retinal detachment with ascertained retinal rupture bears out the hypothesis advanced by previous writers (Weve and Fischer) that the subretinal fluid comes from the vitreous body, the considerable hyaluronic acid content of which has been established (Pirie, Meyer). The fact that the hyaluronic acid concentration in the subretinal fluid seems small at first, and then gradually increases, may contribute to an understanding of the pathogenesis.

Our knowledge regarding retinal rupture and retinal detachment is still scanty, despite the enormous work done by various investigators in their attempts to find the factors giving rise to the lesions. The results of the present hyaluronic acid investigations as well as recent discoveries concerning the liberation of hyaluronidase by allergic vascular or tissue reactions (Mayer and Kull) are of such a nature that it may be tempting, on the basis of them, to *set up a new hypothesis with regard to the pathogenesis of retinal detachment.*

The cases where the pathogenesis is evident, *i.e.*, the traumatic detachments (after perforating injuries, etc.) will here be left out of account. The trauma will often present the character of a triple-response reaction (Lewis-Ebbecke), having many features in common with the allergic vascular reactions.

In other cases of retinal detachment, where direct physical trauma is absent, it may be of value to search for possible psychic trauma in the past history. The possibility of a psychosomatic origin of a disease is gaining ground within many branches of medicine, thereby explaining to an increasing extent why mental conflicts may often give rise to complicated somatic symptoms, presumably *via* certain diencephalically released angioneurotic lesions. The " general adaptation syndrome " recently described by Selye in both physical and mental " stress " likewise contributes to greater clarity. Many eye diseases (glaucoma, iridocyclitis, relapsing superficial keratitis, scleritis, detachments, etc.) of obscure origin may thus be elucidated and explained in a new manner.

Since hyaluronidase is liberated by allergic vascular reactions —as shown by Mayer and Kull—it is reasonable to suppose that an analogous *angioneurotic vascular lesion,* in a portion of peripheral retina, for instance, may cause similar liberation of hyaluronidase. The primary vascular lesion in the retina will involve a *local ischaemia* with consequent tissue necrosis, resulting in *cystoid degeneration,* which sooner or later will *develop into a*

rupture. The liberated *hyaluronidase* within the ischaemic area will *depolymerize the hyaluronic acid* in the adjacent vitreous body, the high viscosity of which will thereby become reduced. The attenuated *vitreous body* may now pass through the retinal rupture. The extent to which the vitreous body *penetrates subretinally*, thereby conditioning the development of retinal detachment, depends no doubt on various factors. A certain balance will occur between the two portions of the vitreous body on both sides of the retinal detachment, and the depolymerization of the hyaluronic acid will stop. Consequently—as demonstrated in the present analyses—we find a somewhat higher hyaluronic acid concentration in cases of more long-standing detachment.

The hypothesis here advanced needs further testing on several points. If it proves possible to apply Mayer and Kull's neutralisation of hyaluronidase, successfully carried out in the skin with antihistamines, to the problem of retinal detachment we may thereby have a chance of supplementing with a causal therapy our current operative treatment, the results of which, as is well-known, are of limited value and merely symptomatic.

Whether we may be justified in drawing certain conclusions with regard to the result of the surgical diathermy treatment on the basis of estimation of the hyaluronic acid concentration in the subretinal fluid is a question which cannot yet be definitely answered. It will be discussed further in a future paper.

In cases of retinal detachment, where an underlying malignant melanoma in the choroid is suspected, we may sometimes fail to reach a definite clinical diagnosis by our present diagnostic aids. The present *hyaluronic acid investigations* suggest that, by analysis of subretinal fluid procurable by simple test puncture, we have obtained a new *differential-diagnostic aid for classification* of the uncertain cases where *malignant tumour* is suspected, because hyaluronic acid is *not* present in the subretinal fluid in cases of malignant melanoma.

Absence of hyaluronidase in the two cases of malignant melanoma does not necessarily exclude the fact that hyaluronidase may have been present at previous stages of the tumour proliferation, as is known from other malignant tumour proliferations. That the violently metastasizing melanomata may be supposed at a certain stage to possess a large hyaluronidase activity is a possibility which requires further investigation.

Summary and Conclusions.

The main features of our present knowledge concerning the nature of the subretinal fluid in retinal detachment, the vitreous body, and the recent biological discoveries of hyaluronic acid and

hyaluronidase are recapitulated. This is followed by a report on present investigations into hyaluronic acid and hyaluronidase in the subretinal fluid in retinal detachments, partly primary with ruptures and partly secondary as a consequence of malignant choroidal melanoma.

Hyaluronic acid and hyaluronidase have been estimated viscosimetrically. In all cases of *detachment with retinal ruptures the subretinal fluid contained a considerable amount of hyaluronic acid*, which, on the other hand, was absent where the detachment was secondary to choroidal melanoma. Hyaluronidase was demonstrated in *none* of the cases.

These observations have prompted a *new hypothesis concerning the pathogenesis of retinal detachment*. The development is now conceived to take place gradually by a primary, vascular retinal ischaemia producing cystoid degeneration with rupture formation, and associated with partial liquefaction of the vitreous body. The liquefaction is caused by local liberation of hyaluronidase, which in turn produces partial depolymerisation of the hyaluronic acid in the vitreous body.

Tests for hyaluronic acid in the subretinal fluid may become of differential diagnostic importance in difficult cases of malignant melanoma with extensive secondary retinal detachment and small primary tumour.

Hyaluronic acid analyses may become prognostically directive for the diathermal treatment of retinal detachment. Since hyaluronidase may be inactivated by antihistamines (Mayer and Kull) the possibility of a supplementary causal treatment with these substances is suggested.

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CHOROIDAL SARCOMA WITH METASTASIS IN THE OPPOSITE ORBIT*

BY

SEYMOUR PHILPS

LONDON

THE history here recorded is that of a woman who, ten years after enucleation of one eye for choroidal sarcoma, developed an encapsulated metastasis in the opposite orbit.

HISTORY

In February, 1938, a lady, aged 59 years, attended the Royal Westminster Ophthalmic Hospital because the right eye had become red and painful. The sight had been failing for a year in this eye, and was only perception of light. She was found to have glaucoma secondary to a large choroidal sarcoma, and the eye was removed (see Fig. 1). Microscopic section confirmed the diagnosis (see Fig. 2).

At this time her left eye was normal, and its corrected vision 6/6. She continued to attend the hospital, but no recurrences arose, and she remained in normal health. Apart from the periodical replacement of her glass eye, nothing unusual happened for nine years.

April, 1947. The patient had an attack of iridocyclitis in the left eye which cleared up completely in one month.

May, 1948. It was found that, whereas the patient had worn a correction of $-2{\cdot}0$ sph./$+0{\cdot}5$ cyl. at 90° with which she saw 6/6, her refraction had now changed, and she achieved normal vision with a $+0{\cdot}5$ cyl. at 90°. While this drop of 2 dioptres of myopia was noted, there was nothing to account for it, and the patient had no complaint, being pleased that her vision had so improved.

October, 1948. The patient noticed that the left eye appeared to be coming forward, and reported to hospital. The proptosis was straight forward, and there was no limitation of movement. This proptosis was variable, and in the following month seemed less marked. X-rays of the orbit revealed no bony changes and the fundus and vision remained normal.

* Received for publication, June 27, 1949.

December, 1948. The proptosis was rather more marked, and a dilated vein appeared in the conjunctiva at the outer canthus. Abduction was slightly limited, and by deep pressure between the globe and the outer bony wall of the orbit a vague resistance could be felt.

It was decided that the left orbit must be explored, and she was told to attend hospital the following week so that she might be admitted, the diagnosis being a tumour behind the left globe, possibly a metastasis.

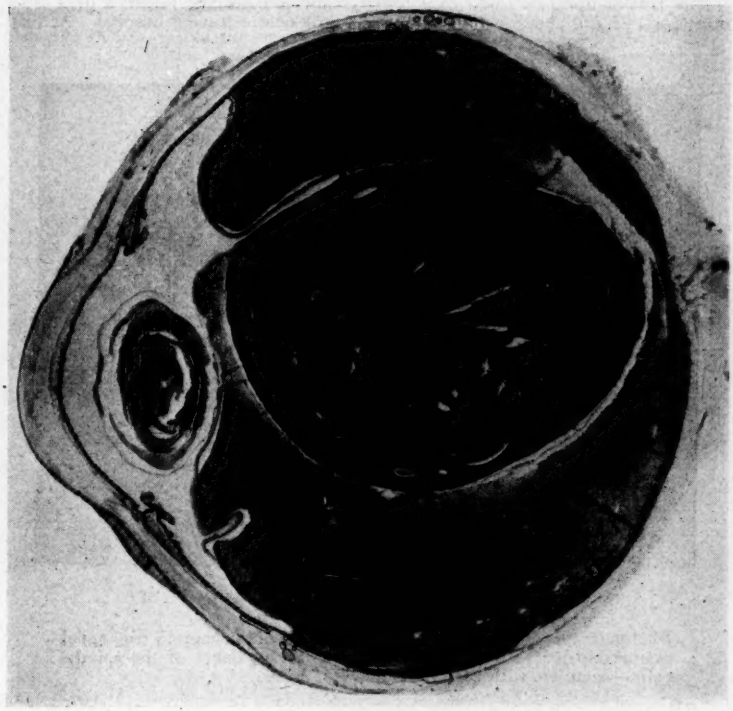

FIG. 1.

Photograph of right eye excised in 1938, showing a large malignant melanoma of the choroid.

The day after this decision had been taken her doctor telephoned the hospital to say that she had been taken acutely ill with a sudden alarming proptosis of the left eye, the cornea of which was exposed so that the lids would hardly meet. She was admitted at once, the diagnosis being haemorrhage into a retro-ocular neoplasm, and the house surgeon performed an emergency tarsorrhaphy.

The swelling and congestion of the left eyelids and orbital tissues remained for three weeks, but, as no blood-staining of the eyelids occurred, the diagnosis of haemorrhage into the orbit seemed less probable, though it was still felt that the bleeding might have occurred into an encapsulated tumour.

January, 1949. Three weeks after admission a left lateral orbital exploration was carried out (Kronlein's exposure), and an encapsulated tumour was found lying within the muscle cone and attached to the under side of the external rectus muscle. After reflexion of this muscle the tumour came away quite easily except at the apex of the orbit, to which it was attached by fibrous tissue which had to be divided. The capsule was accidentally punctured at one stage in the removal with escape of necrotic material, so that a dermoid cyst seemed the most likely diagnosis at this stage. For photograph of tumour see Fig. 3. The position of the tumour is shown in Fig. 3A.

The patient made an uneventful recovery and left hospital nineteen days after operation. Fig. 4 shows the operation scar just before leaving hospital. At that

FIG. 2.

Photomicrograph of the malignant melanoma of the choroid (right eye) removed in 1938. Note the perivascular arrangement of the spindle cells — compare with Fig. 3. H and E. × 306.

time the left vision with −1·0 sph. was 6/6 partly, but one month later she was a little more myopic, and it is interesting to note the return of her myopia when the pressure behind the eye was relieved. She has remained in good health and vision since that time, her vision at this date (June, 1949) being once more, with −2·0 sph., / +0·5 cyl. at 90°, 6/6.

PATHOLOGY.—By Dr. Norman Ashton, Pathologist to the Moorfields, Westminster and Central Eye Hospitals.

Left Orbital Tumour. Pinkish-yellow, ovoid, soft, encapsulated tumour measuring 2·4 cms. × 1·25 cms. × 1·5 cms. (Fig. 3).

Sections. A series of sections taken from different parts of the tumour were stained with haematoxylin and eosin, Van Gieson's stain, Wilder's silver stain and Masson's trichrome stain. Frozen sections were stained with Sudan 111. The

tumour is bounded externally by a dense fibrous capsule, containing voluntary muscle fibres, which merges insensibly with the cellular mass which forms the bulk of the tumour (Fig. 5). Centrally the lesion is completely necrotic, and between the zone of necrosis and the fibrous capsule there is a margin of large polyhedral vacuolated cells supported in a loose fibrous stroma infiltrated with lymphocytes (Fig. 6). In the frozen section stained with Sudan III these cells are seen to contain globules of fat. In the Masson-stained section the structure of the central necrotic area is clearly discernible, and is seen to consist of masses of spindle cells, which are aggregated as a mantle around the thin-walled blood-vessels, with their long axes arranged radially (Fig. 7). Silver staining shows dense pericellular reticulin formation around the large peripheral cells (Fig. 8), but only a few filaments remain within the necrotic area. A small quantity of intra- and extra-

FIG. 3.

cellular pigment is present in the living cell layer. The appearances in the necrotic zone are typical of a malignant melanoma of the choroid, and a comparison with the histology of the tumour of the right eye removed 11 years previously (Fig. 2) leaves little doubt that the orbital tumour is in fact a metastasis from the original growth. The border of large fat-containing cells might be regarded as an inflammatory reaction to the central necrotic mass, but it appears more probable, from a study of the margin of the living and dead tissue, that the whole lesion was originally composed of the same type of cell. In 1912 Ginsberg described three cases in which lipoid degeneration was found in melanotic growths of the choroid: fat was deposited within the cytoplasm of the spindle cells, so distorting and distending them as to form large "foam cells" which, judging from his illustrations, are identical with those in this case. In my view, therefore, this tumour is an encapsulated malignant melanomatous metastasis arising from a primary in the choroid of the right eye and undergoing central necrosis and peripheral lipoid degeneration.

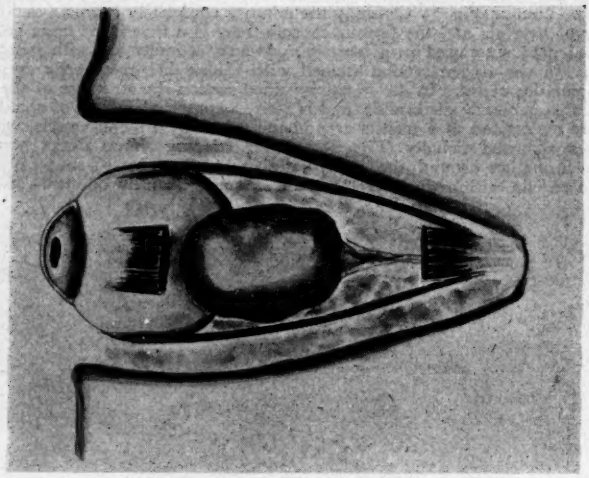

FIG. 3a.

Site of growth within the muscle cone of the L. orbit.

FIG. 4.

FIG. 5.

Photomicrograph of orbital tumour. From left to right can be seen the fibrous capsule containing muscle fibres, the zone of large fat-containing cells and the central necrotic mass of spindle cells. Masson stain X 130

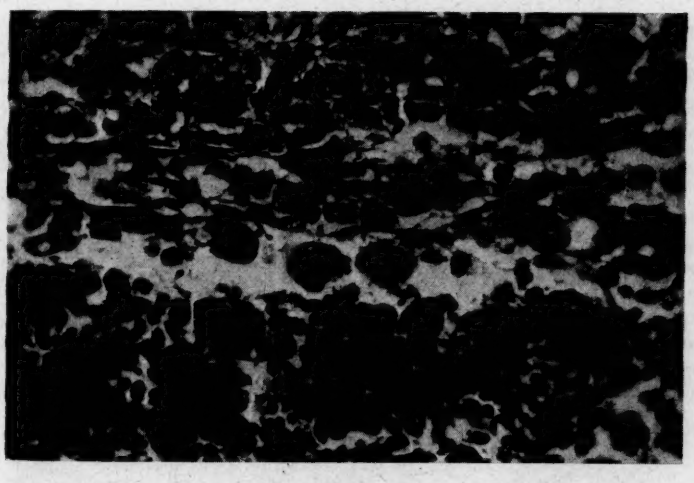

FIG. 6.

Photomicrograph showing the junction of the necrotic tissue below with the margin of large fat-containing cells above. Masson stain. X 410.

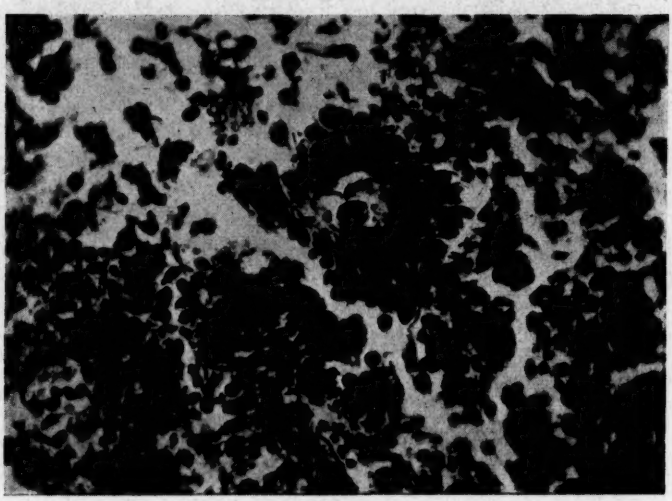

FIG. 7.

Photomicrograph of the central necrotic area showing spindle cells arranged radially around the blood vessels. Compare with the photomicrograph of the original tumour (Fig. 5). Masson stain. × 410.

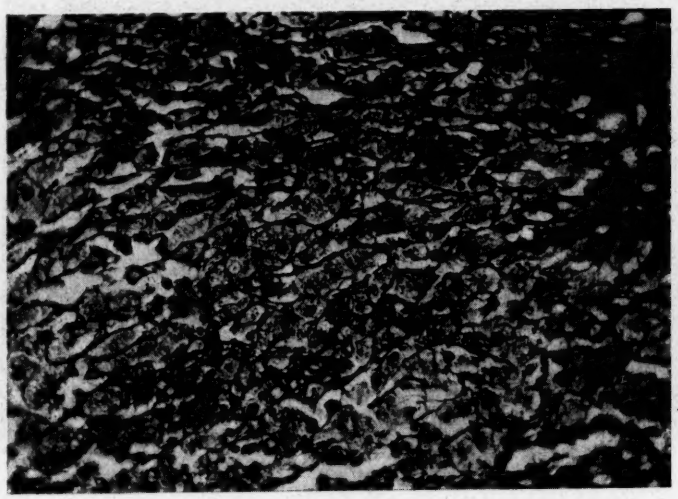

FIG. 8.

Photomicrograph showing pericellular reticulin formation around the large peripheral cells. Wilder's silver stain. ×410.

Conclusions

No instance has been discovered in the literature of a history such as is recorded here, of a woman surviving a large choroidal sarcoma for 10 years, then developing a metastasis in the opposite orbit, which being encapsulated could be completely removed leaving normal vision.

I am grateful to Dr. Norman Ashton for all the trouble he has taken over this tumour, and also to Dr. Hansell of the Medical Illustration Department of the Institute of Ophthalmology for his fine photographs.

REFERENCE

GINSBERG, S. (1912).—*Graefe's Arch. f. Ophthal.*, **82**, 1-57.

HISTO-PATHOLOGICAL STUDIES OF THE BLOOD-VESSELS OF THE EYE*

BY

R. SYSI

HELSINKI

THERE are numerous publications in the literature dealing with arteriosclerotic vascular changes in the eye. Most of them are based on a comparatively small material, which explains the diverging opinions on many points. Thus Koyanagi, Friedenwald and lastly Bergstrand consistently noted more conspicuous changes in choroidal vessels than in those of the retina, while Rintelen observed marked vascular changes in the retina only in few cases. He rarely found any considerable changes in the a. ciliares posteriores, while the others found pronounced sclerosis therein. Rintelen denies the existence of any severe sclerosis in the blood-vessels of the iris and the corpus ciliare, in contrast to Gasteiger and, more recently, Rones, who found great changes in these vessels. There are also differences of opinion as to whether the sclerotic changes spread as far as the anterior parts of the choroid and the retina, or whether they occur only nearer to the posterior pole of the eye. These examples will suffice to show that further studies on vascular changes in the eye are not out of place.

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From the Patho-Anatomical Institute, University of Helsinki.
Chief: Professor Arno Saxen, M.D.

Research workers have as a rule discussed the condition of the eye vessels and their changes in cases of general arteriosclerosis, renal diseases such as nephritis, nephrosclerosis, etc., or when vascular sclerosis of the brain has been present at the same time, but no comparative study has been made of the age-changes occurring in the ocular blood-vessels, when there is no general sclerosis nor any marked local sclerosis in other organs. Thus it is these so-called normal cases that show general wear-and-tear in the vascular system with advancing years.

It was the effect of renal disease in impairing vision that first drew the attention of physicians to the close connection between ocular blood-vessels and those of the rest of the organism (Bright). Clinical experience proved later that many other diseases may give rise to vascular lesions in the eye. Only a few of these ocular changes caused by various general diseases or affections in some other organ come within the scope of the present investigation. Some of these changes we consider physiological, others are on the borderline of the pathological. Some of them occur irregularly, occasionally even in comparatively young individuals, sometimes no traces of them are found even in advanced age, such are gerontoxon, atrophy of the iris and miosis, retinal and choroidal changes, concentric or partial contraction of the visual fields, etc. In other changes, however, such as failing accommodation, we note strict regularity, for this diminution begins in early childhood and nearly always follows the same time-table, to such an extent that a person's age may be determined with considerable accuracy from his accommodative capacity.

Some of these changes must obviously be ascribed to arteriosclerosis. Others again, occurring where there is no arteriosclerosis present, can be explained by changes and wear caused in the tissues by age. A corresponding phenomenon may be noted in many other organs, notably in the blood-vessels. The occurrence of this phenomenon in the blood-vessels does not, however, mean that the wearing-out of the tissue results from vascular changes, but rather that both phenomena arise from the same fundamental cause at the same time, but independently of each other.

When beginning to study the blood-vessels of the eye it is advisable first to note the changes which occur normally in otherwise healthy individuals, before we tackle the question of strictly pathological, arteriosclerotic phenomena. I have therefore collected an extensive control material of cases where no general arteriosclerosis or renal diseases have been diagnosed. Both series have been collected, treated, studied and evaluated in similar circumstances and according to the same principles.

The material studied was taken from 204 corpses, and consists of 408 eyes. The preparations were obtained by dividing the eyes in front of the equator and taking the whole posterior part of the eye with the orbital part of the optic nerve and the surrounding tissue. From the anterior part of the eye the parts within the cornea and sclera were removed for study by detaching them with a spatula, as in the operation of cyclodialysis. The preparations thus include all parts of the eye except the cornea and the 4-5 mm. wide anterior part of the sclera. The preparations were fixed in formalin and stained by van Gieson's method and with elastin. Part of the preparations were also cut with a freezing microtome and stained for fat. We have full clinical records of all the cases, and all the corpses had also been fully dissected.

The distribution of the cases into a control series, arteriosclerotic cases without hypertension, nephritic cases and cases with nephrosclerosis, and into different age groups appears from the following table :—

TABLE 1

Age	0–15	16–30	31–40	41–50	51–60	61–70	71–80	81–90	Total
Control cases	7	9	11	17	23	10	—	—	76
Arteriosclerosis	—	—	—	5	6	6	5	3	25
Nephrosclerosis	—	—	—	7	17	31	17	5	77
Nephritis	1	3	6	4	6	3	3	—	26
Total	8	12	17	33	51	50	25	8	204

Several investigators have noted what was found by us in studying the present material—namely, that the blood-vessels of the eye are subject to the same pathological changes as occur elsewhere in the organism. In different parts of the eye these changes take place with varying intensity and in different relations to each other. Opinions vary in the literature as to what, and how great, changes occur in different parts of the eye. It is therefore not out of place to give a short account of these changes as they appear in the present material.

The optic nerve has two kinds of blood vessels, first, the central retinal artery and vein which pass through the nerve, and secondly, the small pia and septum arteries providing for the nutrition of the nerve itself.

Great changes of the intima are observable in the *arterioles* of the optic nerve, also homogenization and thickening of the wall, and, more often than anywhere else in the eye, complete hyalinization and obstruction of the blood vessel.

In the arteries of the retina, extensive proliferation of the intima and fatty change, also homogenization of the vascular wall occur. In the elastica there are no marked changes. Considerable thickening and increase of the number of nuclei is often noted in the adventitia. In the smallest vessels the changes are especially frequent in the intima. One generally finds that the changes are most

obvious in the retinal parts nearer the papilla, and that they grow less farther away from it. Yet one sometimes notices such changes even in the outermost retinal arteries.

A. ciliares posteriores, which are relatively large blood-vessels, show all these changes in the vascular walls. Besides changes in the intima, severe proliferation of the elastica, delamination and muscular hypertrophy are found. The only actual instance of atheroma occurred in these vessels, and completely obstructed blood vessels are not infrequent.

In the large blood-vessels of the choroid, besides intimal proliferation and fatty change, severe proliferation and delamination and thickening of the muscularis and the adventitia sometimes occur. Changes in the intima and fibrosis are noted in the small vessels, sometimes homogenization. As in the retina, the greatest changes take place in the posterior parts of the eye, but there is less difference in the choroid between the anterior and posterior parts.

In the *corpus ciliare* and in the *iris* the changes are usually slight. Some intimal changes occur, and also fibrosis and homogenization. Here it is more difficult to estimate the changes than elsewhere, since the general hyalinization of the tissues, which sometimes takes place, makes it difficult to distinguish the actual vascular wall from the surrounding tissue. In the iris vascular changes are generally still smaller than in the corpus ciliare. Yet even in the blood-vessels of these organs there is sometimes quite obvious sclerosis.

As well as in cases with arteriosclerosis, changes of this kind occur in the control series, where they must be regarded as normal for every age-group. We know that such changes occur in various parts of the vascular system from childhood, according to recently published statistics on general sclerosis, 8 per cent. in 0-9 year-olds and 23 per cent. in 10-19 year-olds (Eskola).

In the various groups the changes do not differ from each other qualitatively, but they certainly do quantitatively. All parts of the eye have this in common that, when changes occur, their intensity varies greatly even in the same region, so that one finds, side by side, healthy and diseased blood-vessels.

On first comparing the different groups and age-groups one finds that the quality of the changes is easy to estimate exactly, but there are no clearly defined standards by which we can measure the quantity of the changes nor any formula by which they can be expressed exactly, but one has to be satisfied with one's personal observations as regards the intensity of the phenomena and its relation to a change observed in some other vessel.

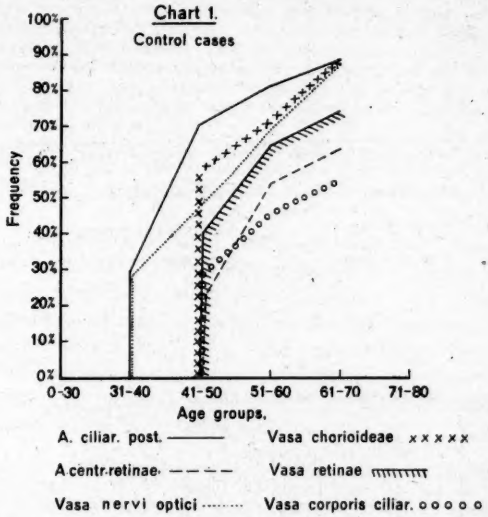
The number of control cases in the material which show no hypertension, no noticeable arteriosclerosis and no renal lesion is 76 (Table 1). Their ages vary from new-born to 70 years.

Under 30 years no vascular changes have been observed in the eyes of the cases in this control series (Chart 1). The changes begin to appear between 31 and 40, and then first in the a. ciliares posteriores and the arterioles of the optic nerve, and even in these in somewhat over a quarter of all the cases. In the next age group, 41 to 50, changes appear in all vascular areas. They are still most frequent in a. cil. posteriores and after that in the blood-vessels of the choroid and in the arterioles of the optic nerve. There are fewer changes in the other regions, least of all in a. centr. retinae and in the blood-vessels of the corpus ciliare. In the following age groups the frequency of the changes in the a. ciliares posteriores, in the vessels of the choroid, and in the arterioles of

the optic nerve increases regularly, reaching about 90 per cent. in the age group 61-71, but being much less in the other groups.

Thus, in the control cases the changes occur most frequently in a. ciliares posteriores, in the choroid, and the arterioles of the optic nerve. It is in these vessels, too, that among the cases examined the changes are clearest and greatest. In other regions, *i.e.*, in the retinal vessels and the corpus ciliare and in the a. centr. retinae the changes are slight. This relation between the intensity of the changes in the different areas is typical of these control cases, where there is no general sclerosis or renal lesion.

Also qualitatively the changes in the control series show special features. The changes mostly occur in the outermost parts of the vessels. In a. ciliares posteriores especially the muscularis and the adventitia thicken, but also the elastica interna may show some thickening though no delamination. The vascular



changes in the choroid are likewise unmistakable, but here also mainly in the outer parts. Fibrosis and homogenization occur to some extent in the smallest vessels. In a. centr. retinae one meets only very slight thickening of the muscles and of the adventitia, and in the small vessels of the optic nerve one may find some homogenization. The changes in the blood-vessels of the retina and the corpus ciliare are extremely slight.

In the material there were 25 cases of arteriosclerosis without hypertension in the 40-90 years age groups (Table 1). General arteriosclerosis occurred in 11 cases, in 19 cases the sclerosis was most advanced in the valves, vessels, and aorta of the heart. It should be noted that the material includes 9 cases with obvious sclerosis of the cerebral blood vessels. The sclerosis in the different organs varied from mild but clearly obvious to the most severe forms.

As regards the vascular changes in the eye we note that their frequency, when compared with that of the former group, is slightly larger (Chart 2). Only in the highest age group, 81-90 years, do we here reach the 100 per cent. limit. This does not mean that patients of this age with arteriosclerosis always had changes in all the vascular regions of the eye, since the number of cases in this group is only 3, which is too small a number for conclusions. This is quite apparent from the following Chart (No. 3), showing a group of cases with

Chart 2.

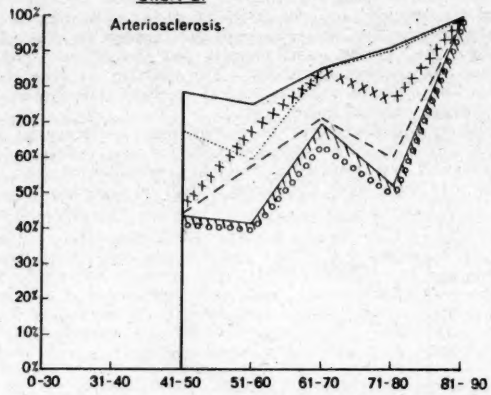
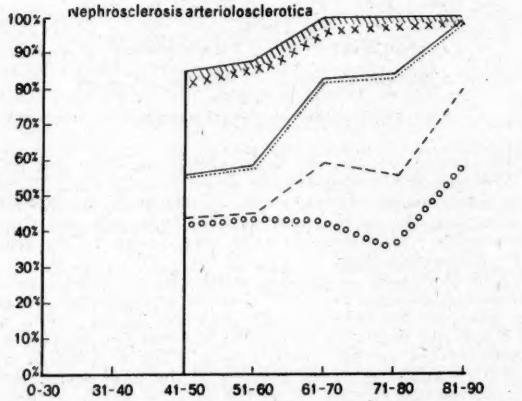


Chart 3.



nephrosclerosis, where even in the highest age group there were some without any changes in the blood-vessels of the corpus ciliare and the a. centr. retinae.

In this chart as in the former, the curves divide into two groups. The curves representing the a. ciliares posteriores, the arterioles of the optic nerve and the choroid together rise high above the others, while the three other curves, forming a group of their own, are much lower. The interrelation between the frequency of changes in the different vascular areas within the group of arteriosclerotic cases is roughly the same as in the control material. The frequency of the changes in the cases with arteriosclerosis is slightly higher in the younger age-groups than in the control cases, but then the rise is less steep. Thus there is no great difference ascertainable in the frequency of the changes between these groups.

The difference in the quality of the changes, on the other hand, is remarkable. Besides the changes noted in the control cases, which were most marked in the outer-most parts of the vessels, intimal changes now become clearly discernible. All the changes are more pronounced and greater than in the preceding group. In the a. ciliares posteriores one can see relatively marked proliferation of the elastica and evident delamination. The changes are most intense in the arterioles of the optic nerve and the choroid, but there is not yet any delamination to speak of in the latter. In a. centr. retinae, in the retina and in the corpus ciliare the changes are still mostly rather small, but with a few exceptions, where rather severe sclerosis occurs.

Although general arteriosclerosis was the rule in the other blood-vessels of the organism in this group of cases, there were several in whom the changes differed neither in quality nor in quantity from those in the same age-groups of the control series.

In this group there were 9 cases of vascular sclerosis of the brain. The relation of this disease to retinal vascular sclerosis must be investigated on the basis of these cases, since in the following group with nephro-sclerosis there is the complication of another disease which may affect the retinal blood-vessels. 6 out of 9 cases in our series had vascular changes in the retina and 7 in the choroid. In two cases, of which one was as old as 72, both the retinal and choroidal vessels were normal.

The number of nephrosclerotic cases in the material is 77 (Table 1), and their age varies from 41 to 90 years. All these cases showed according to the case record a considerable rise in blood pressure, varying between 170 and 280 mm. Hg. In this group the frequency of the changes (Chart 3) was from the first greater in the retinal and choroidal vessels than in the earlier groups. In the other vascular regions, on the other hand, the frequency was approximately the same as in the earlier groups. In the higher age groups the frequency of changes in the choroidal and retinal vessels rose rapidly to 100 per cent. In the others the course of the curves was approximately the same as in the previous ones, and as far as the vessels of the corpus ciliare and the a. centr. retinae are concerned it was lower than for cases with arteriosclerosis.

The grouping of the curves has thus changed. The curves of choroidal and retinal vessels form a group in themselves, with the greatest frequency of changes. Since this fact may give a misleading picture, it is especially important to point out how variable in quantity the changes are. This group contains 4 cases in which the changes are no greater, in any part of the eye, than the changes in quality or quantity occurring in other cases of the same age group. There are, in addition, 3 cases in which the vascular changes in the retina may be placed in the same group as the arteriosclerotic cases of the same age.

Although there is wide divergence in the severity of the changes, they have on the whole increased considerably, especially in the retinal vessels. Pronounced changes are also observed in other vascular regions, but the difference compared with earlier age-groups is smaller in them than in the retina. In other regions,

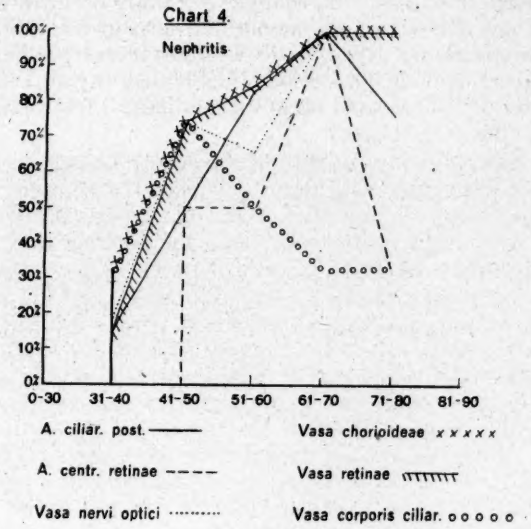
too, the variations in the severity of the changes in the same vascular region are considerable. Both great changes and almost intact blood-vessels may be found everywhere.

The most important difference compared with earlier groups is the remarkable increase in the severity of the vascular changes in the choroid and in the retina while the increase is smaller in other vascular regions. Other authors, and quite recently Bergstrand, have pointed out that in these cases the changes in the choroidal vessels are more severe and occur earlier than vascular changes in the retina. This phenomenon was also obvious in the present material, but with exceptions to the rule in so far as there were certain cases of choroidal changes which fell far below those in the retina in intensity. Yet since there has been no series of excisions on the eyes for investigating this particular point, the apparent exceptions may be due to the fact that the intensity of the changes also varies at different points of the same vascular region.

In the vessels of the corpus ciliare and in the iris the changes are still usually slighter than in other parts of the eye, but this group contains cases where they are conspicuous. As regards the quality of the changes, it is the same as before in this group, but the various types of changes now appear more strongly and clearly. Usually all the layers of the vascular walls are involved in the process. Intimal proliferation, fatty changes, proliferation of the elastica and delamination, thickening of the muscularis and the adventitia are not very pronounced. We even find in the a. ciliaris posterior of a 49-year-old case the only instance of actual atheroma.

In the a. centr. retinae we find changes in all layers of the wall, but they are usually slight. Only rarely was the intima markedly thickened and the elastica delaminated. The arterioles of the optic nerve show relatively great intimal proliferation and one often meets hyalinization and even complete obstruction of the vessel. In the choroid all layers are affected by the process, and the present material contains cases where the elastica also is strongly delaminated, although this phenomenon is otherwise rarer in these vessels than elsewhere. The smallest vessels show advanced homogenization and hyalinization, and obliterated vessels are not uncommon. In the retinal vessels we find marked fatty changes and changes in the adventitia. There are other less obvious changes. The difference between these changes and those observed in earlier groups is so great that it is only in this group that one can speak of unmistakable changes. This does not rule out the existence of obvious changes earlier, but they are not common until we reach this group.

There were 26 nephritic cases (Table 1), and their ages varied from 18 to 80. This group is very heterogeneous and difficult to estimate. Indeed, the group contains cases whose ages vary greatly, cases without diagnosable sclerosis, and cases of severe general sclerosis. All these factors in themselves affect both the picture of the single cases and the frequency chart (Chart 4). The number of the cases is, however, so restricted that to separate the arteriosclerotic cases would mean breaking up the group entirely. Thus all the cases have been treated together, which fact should be kept in mind when estimating the general picture. From a critical point of view we may, however, point out that in this group the changes mostly occur in the vessels of the retina and the choroid and in the a. ciliares posteriores, and they are also frequent in the arterioles of the optic nerve. In this respect the curves have roughly the same course as in nephrosclerosis. However, the greatest frequency occurs in a younger age group than in nephrosclerosis.



The quality of the changes is much the same as earlier, but with this difference that now, besides the changes already mentioned, evident oedema is in some cases observed in the outermost parts of the vessels, which appears as a swelling of the wall, which stains imperfectly. This sign is clear even when no other actual changes are observable.

In the 41-50 years age-group we found retinal vascular changes in the control material as well as in the arteriosclerotic cases. Nephritic cases had changes in the earlier age group, both oedema and fatty changes of the intima. But my material is so small—there are only 4 in the 0-30 age group, and 6 in the 31-40 years group—that we cannot say conclusively that there may not have been changes earlier than in the 31-40 years age group. On the other hand, as even the control series is rather small with 16 in the group 0-30 years and 11 in the age group 31-40, we cannot consider that it sufficiently proves the absence of retinal changes in groups younger than 41-50 years, without actual sclerosis having been diagnosed elsewhere, and with no renal disease present. It therefore still remains open to question whether the changes were actually caused by nephritis. The oedema in the vascular wall may perhaps be considered as an actual nephritic change.

From the facts recorded above, the following points may be emphasised :—

The changes in the control material are slight, occurring mainly in the outermost parts of the blood vessels, and take the form of adventitial and medial thickening, slight fibrosis and sometimes homogenization, rarely slight thickening of the intima, and fatty change.

In connection with arteriosclerosis the changes are usually more obvious, though some cases do not differ from those in the control group. The real difference compared with the control material

is that in arteriosclerosis the changes generally occur in the whole wall and are obvious in the media and also in the intima. Not until arteriosclerosis develops do we find severe proliferation of the elastica, and delamination. Complete hyalinization and obstruction of the vessels occurs sometimes. Atheromatous foci occurred only in one case.

In the quality of the changes nephrosclerotic cases do not differ essentially from cases with arteriosclerosis, but changes are more easily discernible. Nephritic cases have, in addition to the changes mentioned above, oedema in the vascular wall.

The changes both in the control material and in other groups first involve the arterioles of the optic nerve and the a. ciliares posteriores, and afterwards the blood-vessels of the choroid. Changes are rarer in a. centr. retinae and in the retina, and are not demonstrable until severe arteriosclerosis develops. Both retinal and choroidal changes first occur posteriorly, but are occasionally found in the anterior regions of the retina and the choroid. Changes are less frequent in the vessels of the corpus ciliare and the iris than elsewhere in the vascular system of the eye. Thus, though the locality of the changes varies considerably and some vascular areas in the eye are obviously more prone to damage than others, we may say that changes can occur in all the blood-vessels of the eye.

The extent of the changes seems to depend upon where they occur. Generally they seem to be greatest where they appeared earliest, *e.g.*, in the a. ciliares posteriores, in the arterioles of the optic nerve and in the choroidal blood-vessels. The most conspicuous changes were found in the a. ciliares posteriores, which harboured the sole instance of atheroma. In the corpus ciliare and the iris the changes are usually slight.

In all parts of the eye the amount of change varies considerably. Blood-vessels close to each other may differ greatly, one being intact, the next severely damaged, although both belong to the same vascular region of the eye. Likewise the changes vary considerably between different vascular areas. On the other hand there is no marked disparity between the blood-vessels of the left and the right eye.

There is one exception to the rule that the greatest changes occur where they appear earliest, in the mild cases, namely, the changes in the blood-vessels of the retina. In the control cases and in mild cases of arteriosclerosis the retinal changes follow the rule mentioned above, but in more severe sclerosis, nephrosclerosis, and in nephritic cases the changes in the retina are noticeably greater than those elsewhere.

This change in interrelation is especially obvious when the state of the retinal blood-vessels is compared with that of the vessels in the choroid in different groups. In the control cases and in mild sclerosis we find changes in the choroidal blood-vessels without there being anything pathological in the blood-vessels of the retina. Changes in the retinal vessels are always less than those

FIG. 1.

Thickening of the wall of an arteriole of the optic nerve.

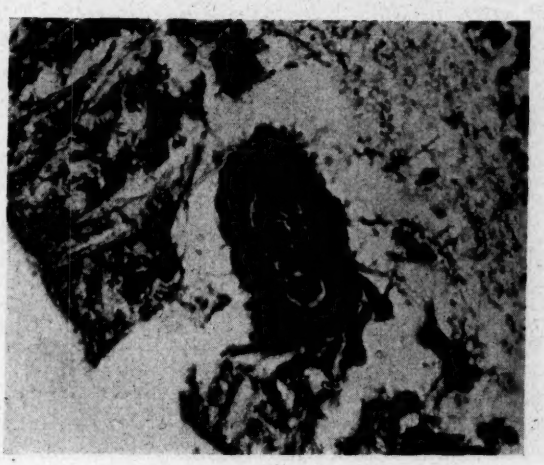


FIG. 2.

Thickening of the wall of a retinal vessel.

in the choroid. On the other hand, in more severe cases of sclerosis, nephrosclerosis and nephritis, the vascular changes in the retina may equal those in the choroid.

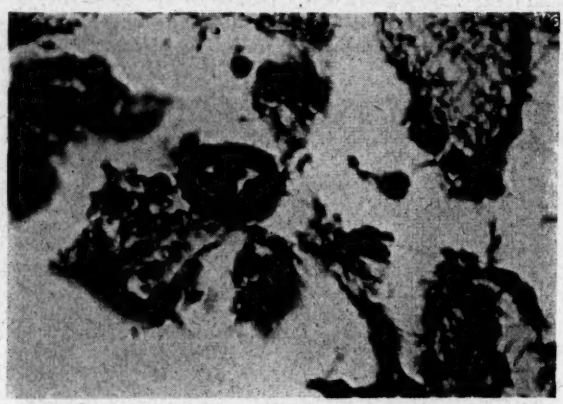


FIG. 3.

Thickening of the wall of a small retinal vessel.

FIG. 4

Atheroma in the wall of an arteria ciliaris posterioris.

FIG. 5.
Fibrosis of a vessel of the choroid.

FIG. 6.
Obstruction of a vessel of the choroid.

FIG 7.

Fibrosis and hyalinisation of the vessels of the ciliary body.

FIG. 8.

Hyalinization of the vessels of the iris.

Concerning the frequency of the occurrence of the changes, we notice that in the present material they begin to appear after the age of 30, and the incidence then increases evenly. In the group of normal changes and in cases with arteriosclerosis the curves (Charts 1 and 2) divide into two fairly distinct groups, of which the curves of the a. ciliares posteriores, the arterioles of the optic nerve and the curves of the choroid form the upper group, while the frequency curves showing vascular changes in the a. centralis retinae, the retina and the corpus ciliare run in a separate group lower down.

When we come to the groups of nephrosclerotic cases and those with nephritis, we have a different grouping of the curves (Charts 3 and 4). It is the retinal changes that now show the greatest frequency and the corresponding curve has the highest peak. In the a. centralis retinae and in the blood-vessels of the corpus ciliare the frequency of changes remains relatively low in all groups. A renal lesion does not seem to have any appreciable effect on these vessels. As to diabetes, which is known to cause changes in the pigment epithelium of the iris (*Deutschman, Kamochi*), the present material does not warrant any conclusions, for it contains very few cases of diabetes.

From a comparison between the results derived from the present material and those recorded in the literature we would make the following points. In contrast with Rintelen we find frequent and great changes in the a. ciliares posteriores. Nor can we agree with his theory that changes are rare and usually small in the region of the corpus ciliare. My material seems to support the view of many other authors, *e.g.*, Gasteiger, Mylius and Rones, that considerable changes are found here.

My series also supports the findings of Koyanagi, Friedenwald and Bergstrand that severe sclerosis occurs in choroidal blood-vessels. The material contains some severe cases of nephro-sclerosis in which the vascular changes in the choroid, though pronounced, are yet slighter than those noted in the retina. We also note, as did Rintelen, Bergstrand and others, that sclerosis of the retinal vessels may extend as far as the ora serrata, though Mylius had earlier declared that sclerosis is limited to the posterior retina.

The oedema in the vascular wall, found in cases with nephritis, supports Wagener's statement that it is possible to differentiate between the retinopathy of glomerular nephritis and that of essential hypertension. On the other hand we find that even arterio-sclerotic changes are relatively frequent in the blood-vessels of the nephritic group.

My material also supports Volhard's statement that the retina reflects the condition of the kidneys. Advanced changes in the retinal blood-vessels imply the existence of similar changes in those of the kidney, but healthy vessels in the retina are not proof against disease in the renal blood-vessels. Raehelmann's theory that the blood-vessels of the retina reflect the condition of the cerebral blood-vessels has earlier been disproved, and is further contradicted by the present material.

Summary

The material consisted of 408 eyes taken from 204 corpses. It was divided into four parts: the control series, including those cases in which no clinical signs of sclerosis had been recorded, cases with arteriosclerosis, those with nephrosclerosis, and nephritic cases.

The changes noted were always comparatively slight in the a. centralis retinae. In the arterioles of the optic nerve, on the other hand, we found extensive changes, and these blood-vessels were often obstructed. The changes were likewise considerable in the a. ciliares posteriores, wherein atheroma and frequent obstruction occurred. The third region where the changes were often extensive was the choroid. The vascular changes in the retina were as a rule slight in the control material and in cases with arteriosclerosis, while in the nephrosclerotic cases and sometimes in nephritic cases they were more pronounced. Vascular changes occurred even in the anterior parts of the retina. The changes were usually slight in the blood-vessels of the corpus ciliare and the iris.

The changes were of the type usually occurring in sclerosis, with the exception of the oedema in the vascular wall which was noted in nephritic cases.

Among the control cases and those with arteriosclerosis, the frequency of the changes was greatest in the arterioles of the optic nerve, in the a. ciliares posteriores and in the blood-vessels of the choroid. In cases with nephrosclerosis and nephritis the greatest frequency occurred in choroidal and retinal blood-vessels. In the control material the frequency of the changes did not exceed the 90 per cent. limit even in the oldest age-groups.

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CONVERGENCE*

An investigation into the normal standards of age groups

BY

A. MELLICK

GLASGOW

A SURVEY of the literature reveals that there is considerable discrepancy as to the normal values of the horizontal ductions of the eyes. Table I analyses the results obtained by various authorities. It will be seen that the results vary widely, and difficulty is encountered in explaining these divergent findings. Unfortunately comparison between the conclusions of different observers is rendered difficult, since in many instances no mention is made of the type of instrument employed, or of the kind of target used.

The present investigation represents an attempt to establish the normal range of ductions. For this purpose, the following procedure was adopted.

TABLE I.—*Duction Values by Various Observers*

Figures are in prism dioptres

Author	ABDUCTION		ADDUCTION	
	Distance	Near	Distance	Near
A. Græf		5-10		30 or more
Berens, Losey and Hardy ...	6	16 19	16	38-41
C. Sheard				30
M. Dobson	8	18	24	30
Weymouth, Brust and Gobar		17		20
S. V. Abraham		21		19
G. H. Giles	7-8	16-18	24	24
L. C. Peter	+8		15-18	
N. A. Stutterheim			50	
J. Maxwell				18
Scobee and Green			19	

Certain criteria were essential in the selection of cases. It was in the first place, necessary to exclude any subject who suffered from gross ocular disease. The material was derived from the outpatients of the Glasgow Eye Infirmary, and the major portion consisted of those who had been treated for, and had recovered

* Received for publication, July 14, 1949.

from, such minor disabilities as conjunctivitis and chalazion. The residual group comprised those who attended for correction of errors of refraction, provided the latter did not exceed 4 dioptres of hypermetropia or myopia. Furthermore, the presence of heterophoria rendered the individual unsuitable for inclusion in the survey. The group, accordingly, cannot be taken to represent a complete cross-section of the community, but it does offer a reasonable basis for the object in view. The effect of age obviously merits special study, and accordingly the results have been analysed in terms of age groups.

A wide variety of instruments for testing ductions is available. Broadly speaking, these utilise one of two principles. One type is based on the principle of applying gradual increase of prism power, and is represented by the variable prism stereoscope. In the second type of instrument, two fused images are separated or approximated by rotating the slide-carriers of the synoptophore. Both principles were adopted, so that comparison of the results of the two groups could be obtained, each patient being tested with the variable prism stereoscope and the synoptophore.

The possible influence of the nature of the target requires further investigation, but in the present study, use was made of only two targets. One was a simple flat fusion target, and the other was a stereoscopic target of the bucket type. With the variable prism stereoscope, the target at distance was a letter of the 6/6 or 6/9 line of Snellen type; while at near, the line of letters on the Sheard card was employed. For measuring the ductions at distance with the stereoscopic target using the variable prism stereoscope, the pictures were placed in the instrument with +3·00 dioptre lenses in the eye-pieces, and these were removed for measuring the corresponding ductions at near.

Measurements were taken after the existing error of refraction had been corrected. The inter-pupillary distance of each patient was measured, the distance phoria was read on the Maddox tangent scale, and the Maddox wing was used for measuring the near phoria. Examination of the subject was completed with one

TABLE II

Distribution of patients in age-groups

Age	0-20	21-30	31-40	41-50	51-60	61+	Total
Number	115	128	96	116	53	53	561

instrument before testing with the other, the variable prism stereoscope usually being first employed. In the event of any persistence of convergence after measurement of adduction, sufficient time was allowed to permit of relaxation.

Observations were made on 561 subjects. The numbers in the respective age groups are shown in Table II.

TABLE III.—*Variable Prism Stereoscope*

ABDUCTION

Mean Values and Standard Errors

Prism Dioptres

Measures	Age 0-20 years	Age 21-30 years	Age 31-40 years	Age 41-50 years	Age 51-60 years	Age 61+ years	All Ages
D1 ...	8·2±0·2	8·2±0·3	7·8±0·3	7·8±0·2	7·9±0·3	7·5±0·3	7·97±0·10
D2 ...	9·0±0·4	8·6±0·4	8·5±0·4	9·2±0·3	9·7±0·4	9·5±0·3	9·09±0·15
N1 ...	13·2±0·3	13·8±0·4	13·7±0·4	13·9±0·3	14·3±0·5	12·6±0·5	13·61±0·16
N2 ...	11·7±0·3	11·9±0·3	12·7±0·4	12·3±0·3	11·8±0·4	11·7±0·4	12·04±0·15

TABLE IV.—*Variable Prism Stereoscope*

ADDUCTION

Mean Values and Standard Errors

Prism Dioptres

Measures	Age 0-20 years	Age 21-30 years	Age 31-40 years	Age 41-50 years	Age 51-60 years	Age 61+ years	All Ages
D1 ...	18·0—0·6	17·0±0·6	16·6±0·6	18·1±0·6	17·8±0·7	19·5±0·8	17·68±0·26
D2 ...	17·8±1·7	16·5±1·0	16·0±1·4	18·2±1·1	18·9±1·3	22·6±1·1	18·29±0·50
N1 ...	26·5±0·9	25·8±0·8	27·6±1·1	26·3±0·8	25·0±1·3	27·3±1·1	26·42±0·39
N2 ...	21·9±0·9	21·7±0·7	21·3±0·9	21·9±0·8	22·0±1·1	26·1±0·9	22·18±0·36

Tables III to VI summarise in tabular form the results obtained, analysed in their various age-groups, together with their standard errors; while in Table VII, the combined results for all ages are given. In the tables, D represents the duction at distance, N the duction at near, 1 represents a flat target, and 2 a stereoscopic target. All results are expressed in prism dioptres. Table VIII shows those groups where significance, or bordering on significance, has been established.

TABLE V.—*Synoptophore*

ABDUCTION

Mean Values and Standard Errors

Prism Dioptres

Measures	Age 0-20 years	Age 21-30 years	Age 31-40 years	Age 41-50 years	Age 51-60 years	Age 61+ years	All Ages
D1 ...	10·4±0·2	11·0±0·3	11·1±0·3	11·0±0·3	10·5±0·4	10·2±0·4	10·78±0·12
D2 ...	12·2±0·4	11·9±0·4	11·9±0·4	11·6±0·3	11·5±0·4	11·2±0·5	11·77±0·16
N1 ...	12·5±0·3	12·8±0·3	13·5±0·4	12·9±0·3	11·7±0·4	11·5±0·4	12·63±0·13
N2 ...	13·9±0·4	13·3±0·4	13·9±0·4	13·5±0·3	12·7±0·5	12·0±0·5	13·36±0·16

TABLE VI.—*Synoptophore*

ADDUCTION

Mean Values and Standard Errors

Prism Dioptres

Measures	Age 0-20 years	Age 21-30 years	Age 31 40 years	Age 41-50 years	Age 51 60 years	Age 61+ years	All Ages
D1 ...	37·8±1·2	39·3±1·7	40·8±2·2	36·4±1·6	35·8±1·8	40·9±1·7	38·47±0·76
D2 ...	39·3±1·9	42·2±1·9	42·2±2·2	37·0±1·6	39·3±1·9	42·1±1 4	40·33±0·79
N1 ...	51·9±1·4	53 7±1·9	55·4±2·1	47 4±1·9	48·2±2·5	48·9±2·1	51·36±0·83
N2 ...	50·6±1·8	54·3±2·0	55·0±2·5	48·3±1·8	48·9±2·1	51·0±1·9	51·68±0·86

Influence of Age.—From an examination of those rows of Tables III to VI where significance (or bordering on significance) has been established, the following results are obtained:—

Variable Prism Stereoscope:—

Adduction D2. Apart from age group 0-20, the means show a progressive increase as age increases.

Adduction N2. The significance is due mainly to the influence of age group 61+.

Synoptophore:

Abduction N1. The means increase in value up to age group 31-40, followed by a progressive falling-off as age increases.

Abduction N2. The means remain steady up to age group 41-50, and then decline for the remaining two groups.

Adduction D1. A progressive increase to ages 31-40, and then a decrease for the next two groups, followed by a rise for ages 61+.

Adduction N1. A progressive increase to ages 31-40, but the remaining groups are more or less steady at a much lower level.

The above analysis does not appear to show any general law regarding the influence of age on the measurements. When this finding is coupled with the fact that where significance has been established for any one row of tables III to VI for one type of instrument, there is no corresponding significance for the other type, it would appear that, while noting the significance, no particular importance should be attached to it. It is therefore assumed that all ages can be combined, and the mean differences between the two types of target can now be discussed.

Influence of type of target.

Table VII gives the means for all ages, with the two types of target. In order to find whether there was any significant difference between D1 and D2, and between N1 and N2 for abduction and adduction for each of the instruments used, Table IX was drawn up; this gives the results of the analysis.

TABLE VII

Mean Values and Standard Errors, All Ages

Prism Dioptres

	Variable Prism Stereoscope		Synoptophore	
	ABDUCTION	ADDUCTION	ABDUCTION	ADDUCTION
D1	7·97±0·10	17·68±0·26	10·78±0·12	38·47±0·76*
D2	9·09±0·15	18·29±0·50*	11·77±0·16	40·33±0·79
N1	13·61±0·16	26·42±0·39	12·63±0·13*	51·36±0·83*
N2	12·04±0·15	22·18±0·36*	13·36±0·16*	51·68±0·86

*Significance or bordering on significance.

The differences were tested by the use of the formula

$$\text{Standard error of differences} = \sqrt{S_1+S_2}$$

where S_1 and S_2 are the standard errors of the means of the component parts, as given in tables III to VI.

Where, however, this method did not yield significant differences, the more rigorous method of using individual differences was used; that is to say, if D1 and D2 were to be compared, the difference D1-D2 was calculated for each

individual. The standard errors computed in this way do not thus include variations due to differences in individuals.

TABLE VIII

Differences between Means of any one row of Tables III—VI for different ages

	Variable Prism Stereoscope	Synoptophore
ABDUCTION		
D1	No Significant Difference	No significant Difference
D2	No Significant Difference	No significant Difference
N1	No Significant Difference	Significant Difference
N2	No Significant Difference	Significant Difference
ADDUCTION		
D1	No Significant Difference	Bordering on Significance
D2	Significant Difference	No Significant Difference
N1	No Significant Difference	Significant Difference
N2	Significant Difference	No Significant Difference

TABLE IX

The Differences D1-D2 and N1-N2 (all ages)

Prism Dioptres

Variable Prism Stereoscope			Synoptophore		
ABDUCTION			ABDUCTION		
D1	...	7·97	D1	...	10·78
D2	...	9·09	D2	...	11·77
D1-D2	...	-1·12*	D1-D2	...	-0·99*
N1	...	13·61	N1	...	12·63
N2	...	12·04	N2	...	13·36
N1-N2	...	+1·57*	N1-N2	...	-0·67*
ADDUCTION			ADDUCTION		
D1	...	17·68	D1	...	38·47
D2	...	18·29	D2	...	40·33
D1-D2	...	-0·61	D1-D2	...	-1·86
			(bordering on significance)		
N1	...	26·42	N1	...	51·36
N2	...	22·18	N2	...	51·68
N1-N2	...	+4·24*	N1-N2	...	-0·32

* Significant Difference

Table IX shows that significant difference in the two types of target is present in most but not all of the ductions tested. These differences were not all in the same direction, nor, from the practical point of view, could they be considered as being great.

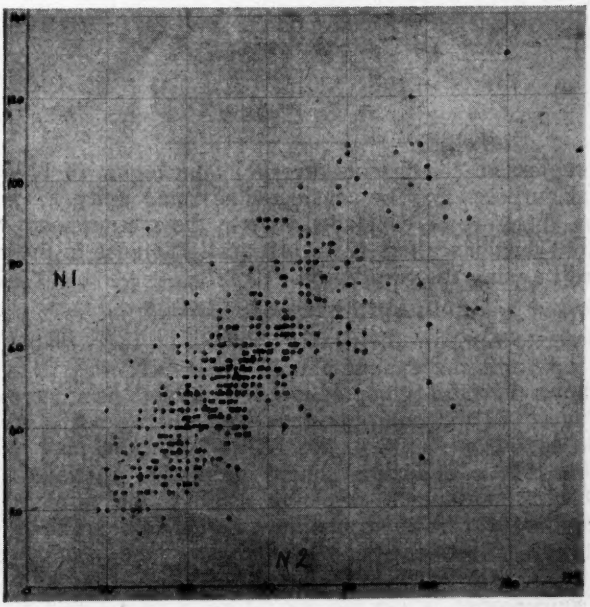
TABLE X

Regression Co-efficients
a and c where
D1=a D2; N1=c N2; for all ages

	Variable Prism Stereoscope	synoptophore
ABDUCTION		
D1 = a D2	0·81	0·91
N1 = c N2	1·15	0·94
ADDUCTION		
D1 = a D2	0·98	0 97
N1 = a N2	1·20	1·01

TABLE XI

Relationship between N1 and N2
Synoptophore, all ages, adduction
Prism Dioptres



Regression Co-efficients.—Assuming that there was a constant relationship between D1 and D2, and between N1 and N2, the regression co-efficients were calculated for the various age groups, based on the formulae

$$D1 = aD2$$
$$N1 = cN2$$

where a (or c) measures the ratio of D1 to D2 (or of N1 to N2).

Table X gives the results of these calculations, which were found to fit the data very well. Table XI demonstrates one graph constructed to show the relationship between N1 and N2 adduction, for all ages on the synoptophore.

TABLE XII

ALL AGES

Ratio : $\frac{\text{Synoptophore}}{\text{Variable Prism}}$

ABDUCTION	
D1	1·35
D2	1·29
N1	0·93
N2	0·98
ADDUCTION	
D1	2·18
D2	2·21
N1	1·94
N2	2·33

The regression co-efficients are all in the region of 1, and for practical purposes may be considered as being unity.

It can therefore be concluded that in the measurement of the horizontal ductions, there is no practical difference in the results obtained in using the two types of target.

Comparison of results on the two instruments.

In order to compare the results obtained on the variable prism stereoscope and the synoptophore, Table XII was drawn up. This shows the ratio Synoptophore : Variable Prism Stereoscope for all ages. In abduction, the ratio varied between 0·93 and 1·35, while in adduction the range was 1·94 to 2·33. One may conclude therefore, that in abduction similar results are obtained at near on the two instruments; while at distance the results on the synoptophore will be about one-third higher in value than on the variable prism stereoscope. In adduction the results on the synoptophore will be about double those obtained on the variable prism stereoscope.

SUMMARY

561 subjects were examined on the synoptophore and variable prism stereoscope, and their horizontal ductions were compared from the point of view of age and 2 types of target. The effects of age and of both types of target were found to be slight.

Difference in the results obtained on the two instruments are described and analysed.

The above investigation was carried out with the aid of a grant from the Spencer Research Fund. I have to thank Dr. R. A. Robb, of the Mathematics Department of the University of Glasgow, for the statistical work.

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ADENO-CARCINOMA (MIXED TUMOUR) OF THE LACRIMAL GLAND*

BY

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THE total number of " mixed " tumours of the lacrimal gland hitherto reported appears to be less than three hundred, so any new case is still of importance. The case here described presents certain special features not without interest.

The commonest story is that of a patient complaining of a lump under the outer part of the upper lid, over which the skin is freely moveable. This may or may not be accompanied by exophthalmos, diplopia and loss of vision. Treatment consists of local removal, and in the majority of cases there is no recurrence.

Such tumours sometimes show local malignancy, and may bring about the death of the patient after repeated operation or extenteration of the orbit. A fatal termination may also be due to direct spread, in one case to the meninges and involving the cervical glands (Jack and Verhoeff). Lane found metastasis in seven out

* Received for publication, April 13, 1949.

of ninety-five cases, and Godtfredsen found metastasis in lymphatic glands in three out of ten cases. Mr. Dickson Wright tells me that he knows of five or six cases in which general dissemination, especially involving the liver, has taken place.

Now that the elements suggesting mesodermal origin are explained as arising from the metaplasia of epithelial cells, and that this explanation has been accepted, all the varied nomenclature and varieties based on the presence of mesodermal tissues become inaccurate and outdated. They will, however, continue to serve to stress the degree to which metaplasia is possible.

The tumour removed from the case here recorded has been examined and described by Mr. T. H. C. Benians, and his report is published herewith. He has also supplied some excellent microphotographs, two of which show a mass of tumour cells being squeezed into a cone with blood from a ruptured capillary, and lying free in a gland compartment (Figs. 4 and 5). This, we consider, might provide both explanation and cause of dissemination by the blood stream.

A healthy-looking girl, aged nineteen years, came to my out-patients on September 4, 1946. She was suffering from marked proptosis of the left eye, and she gave a history that this had first been noticed two years ago, but had increased materially during the past four months. The protrusion amounted to about a fifth of an inch. There was no divergence, but, as the photograph suggests, the depression usually found in a proptosed eye, may have been somewhat greater than usual; there was no diplopia, no suggestion of conjunctival or other inflammation or congestion, and, apart from the prominence of the eye and pain for the last two days, the patient had no complaints.

Vision of the right eye was 6/5, and of the left 6/9, and there was no field defect. Vision with the left eye later became subject to fatigue with intermittent blurring. Both eyes were slightly and similarly hypermetropic, but correcting lenses made no difference to the visual acuity. The pupils were equal and active, the media clear, and the only abnormality within the eye was slight left papilloedema without any haemorrhages. Palpation around the globe revealed no resistance, but it seemed evident that a tumour must be present, presumably within the cone of muscles, and a provisional diagnosis of meningioma of the optic nerve was made.

An X-ray picture taken by Dr. Cochrane Shanks to show the optic foramina, indicates no disparity. Other photographs show no sign of the tumour. I referred the case to Mr. Eugene Wolff for his opinion, and he agreed with me in thinking that a meningioma of the optic nerve was the most likely diagnosis. The outward appearances are well shown in the accompanying photographs (Figs. 1, 2, 3).

She was admitted to hospital and I asked Mr. Dickson Wright to see her with a view to operation; it was decided that the orbit should be explored from above, after a left frontal craniotomy.

Mr. Dickson Wright has given me the following description of the operation:

December 12, 1946. "Lt. frontal craniotomy (Mr. Dickson Wright). G.A. (Dr. Cave).

1. Trotter flap—Burrs and Gigli saw. Hinged on temporalis muscle.
2. Orbital roof thinned—removed.
3. Whole supraorbital ridge resected in one piece with Gigli saw and restored to its place after the removal of tumour.
4. Resection of tumour of lacrimal gland which extended backward to apex of orbital cavity. Removed intact with surrounding tissue. Levator palpebrae muscle and possibly its nerve-supply damaged.
5. Closure in layers. Dural hitch sutures to avoid epidural clot. Small temporal drainage tube.

FIG. 1.
Full face.

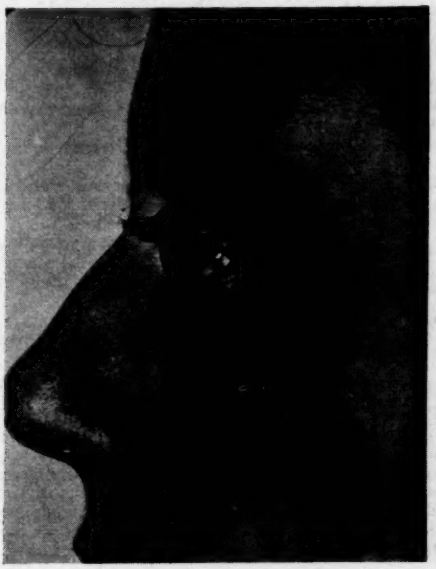

FIG. 2.
Side view of affected eye.

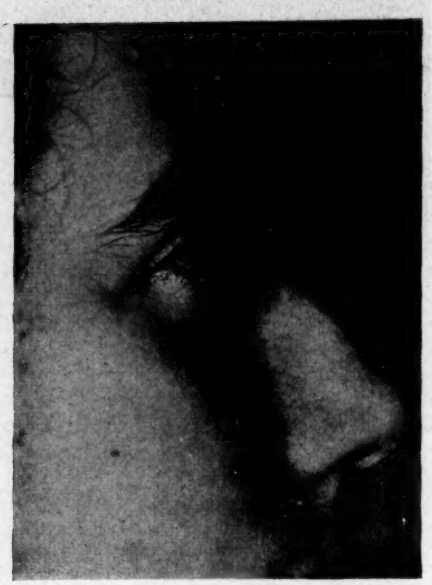

FIG. 3.

Side view of unaffected eye.

December 21, 1946. Stitches and tube removed."

Mr. Dickson Wright did not see the normal gland separately and considers that a tumour of this size would have obliterated it.

X-ray treatment was carried out by Mr. Anthony Green, who makes the following comments:—

"In view of the fact that similar tumours in the parotid gland had proved sensitive to irradiation in many instances, it was considered well worth while giving treatment, provided the eye could be adequately screened.

"A plaster-cast model of the head was made, and a wax mould fitting to the face so that the X-ray beams were carefully directed to the site of the growth. A small protective piece of lead rubber was built in to the wax so that direct irradiation to the globe was avoided as far as possible.

"Tissue dose calculated at the lacrimal gland 4,783r. in 4 weeks.

"The eye was slightly sore after the treatment, but the reaction cleared up quickly, and the oedema of the eye settled down."

Mr. T. H. C. Benians reports as follows:—

A rounded flattened tumour 3½ x 1½ cm. with a thin fibrous capsule and irregular bossy surface. It is firm and elastic, showing on section an opaque yellowish-white mottled surface with occasional fibrous strands and apparently very scanty blood-supply, though a few small subcapsular haemorrhages are present. The lacrimal gland was not identified. Without entering into the discussion on origin and nomenclature that has for many years centred on growths of similar type arising mainly in the salivary glands, one can say that the microscopic picture is that of an adenoma with patches of "mucoid" degeneration (Cystic basalioma of Godtfredsen; Pleomorphic adenoma, Willis). Structurally it shows some large

parenchymatous areas in which the cells have either a solid acinar or a cribriform arrangement (Fig. 4), the latter showing few or many pseudotubular or acinar spaces filled with a palely staining eosinophilic hyaline substance. Other areas are composed of small cysts or dilated acini similarly filled. Elsewhere single or grouped tubules lined by radially arranged cells, sometimes in two layers, form separate entities of more normal anatomical type. The tumour-cells are moderately uniform in size and pale, with a round nucleus of relatively large size which shows a well marked chromatin network and one or more nucleoli. Some cells contain small droplets of hyaline material, and a small proportion are of giant size hugely distended with hyaline droplets. The latter are found only in the more anaplastic parts of the growth.

Vascular spaces are abundant in some areas, and mostly contain blood. They lie in the stroma usually close to the gland element, and are formed of a single layer

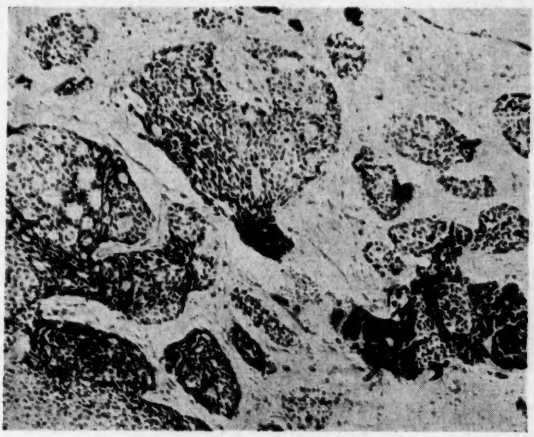

FIG. 4.

Showing general adenomatous structure of growth with torsion effects (×75).

of fine endothelial cells; a few large, better formed vessels traverse the structure of the gland.

The intimate stroma is of denser bands of collagen than the capsule, and tends to divide the parenchyma up into more or less regular large or small compartments. In the larger masses of cells the collagenous supporting structure is entirely absent. The "mixed" element of the tumour is rather scanty, and consists of irregular patches of hyaline material in which scattered epithelial cells can still be recognised. This material blends with and may ablate both the cellular and collagenous elements of the growth.

The capsule, or more probably false capsule, is thin and made up of collagen fibrils with here and there intercalated compressed tumour-tissue. The part of the gland examined close to the capsule shows in several places the effect of torsion or pressure on the tumour cells, which have assumed a spindle-shape and stain densely. A block of such cells is seen forced into a cone and lying free mixed with blood in an adjacent compartment (Fig. 5).

Sections of the tumour show a remarkable amount of this cell distortion, some of it in small patches deeper in, as though force had been exerted through a band of stroma traversing the region. Tearing of the thin-walled vascular spaces was observed. If these changes occur during operation, dissemination by the blood

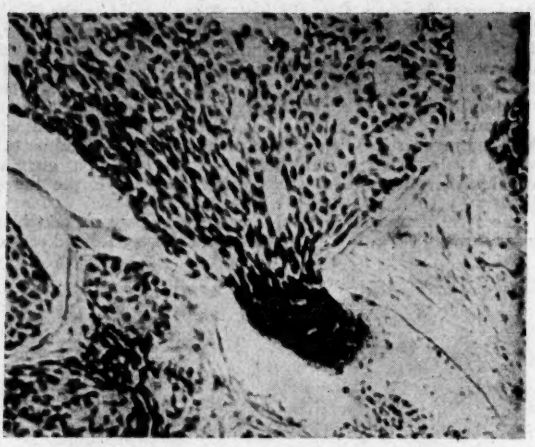

FIG. 5.

Higher power picture of same (×300).

stream would no doubt be possible, and since the growth was removed by free exposure after raising the orbital roof and presumably without undue trauma, it seems that the cells of this tumour may be of a very soft, almost diffluent character.

From the strictly histological standpoint, and judging by the usual criteria, this tumour would appear to be benign, but it is clear from Godtfredsen's paper that growth behaviour in this group is not consistent with microscopical structure, and that these tumours must be regarded as essentially malignant.

In Fuchs' Diseases of the eye, one finds the statement: " New growths of the lacrimal gland are mostly mixed tumours in which the connective tissue of the gland as well as the epithelial portion participates. As indeed the one or the other part predominates in the histological pictures one speaks of fibroma, myxoma, lymphoma, sarcoma or of adenoma, carcinoma or cylindroma."

Morax in his Pathology stresses the slight vascularity and small amount of protoplasm, also the hardness, due to great development of supporting tissue, encapsulation and yellow colour of the tumour.

Seen again in October, 1947, the patient appeared to be in excellent health. Her only complaint was that the left eyebrow, which had been shaved, had failed to grow again. The left eyelid drooped somewhat, but not enough to cover the pupil. She had no diplopia and no pain, and it is interesting to note that she had not suffered from dryness of the eye, even in the hottest weather. The left eye had developed some hypermetropic astigmatism (+2·50 D.S. with +1·75 D.C. Axis 70), but when this was corrected, vision proved to be 6/9 as before operation. The fundus was normal. There was no sign of secondary growths in glands or liver.

I saw her again on May 23, 1949, and found that she had been practically bedridden for six months. She keeps her bed partly because of weakness but chiefly because any form of exertion causes her to be sick. She is very thin.

The left eye is exophthalmic, the lower two-thirds of the cornea being keratinised, vascular and opaque, and the fundus can be seen only dimly through the remaining part. It was possible to make out that the disc was swollen. The orbit is evidently filled with a recurrence which projects forwards above the eye, where it is very hard and tender. The eye has been immobilised for some time past, presumably through involvement of the nerves at the back of the orbit, and during the last month the right eye has been similarly involved, but the optic disc is normal, and there is no evident loss of vision. The lid droops, the pupil is semi-dilated, and the eye cannot be moved in any direction. There is no evidence of any secondary growth, but the abdominal wall was found to be somewhat rigid. Her doctor tells me that she eats very little and it is evident that her weakness is progressive.

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THYROIDECTOMY AND THYROTROPIC EXOPHTHALMOS (EXOPHTHALMIC OPHTHALMOPLEGIA)*

A Review of 1001 Thyroidectomies

BY

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IT has been noted since the early days of thyroid surgery that the exophthalmos of primary thyrotoxicosis (Graves' disease) did not always subside following an otherwise successful thyroidectomy, but that in certain cases it even progressed. Benedict and Knight (1923) of the Mayo Clinic described a case of progressive exophthalmos following thyroidectomy performed six months previously, and there are now many other reports in the literature of this sequence of events. Zimmerman (1929) recorded 11 cases in which this condition followed thyroidectomy, and in Russell Brain's (1944-45) series of 61 cases there were 11 which were post-operative. Mann (1946) in a series of 18 cases observed during the war years, reported 7 post-thyroidectomy cases. Robertson (1945) reported 9 similar cases with the loss of both eyes in two cases and the loss of one eye in two other cases. With similar cases being reported in increasing numbers, it began to appear that thyroidectomy was associated with a definite risk of thyrotropic exophthalmos. Robertson (1945) states that he does not

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think he would operate on a patient over 40 years of age who, in addition to exophthalmos, showed lid oedema.

In this apparent increase in the incidence over the last few years two factors were probably operating. The first was that the condition was now recognised as a clinical entity, distinct from the exophthalmos of primary Graves' disease, and as such, appeared in the literature. The second, and more problematical, was that the increase was due to some other factor such as the emotional stress of the war. In support of this Mann and Russell Brain both found a history of psychic trauma to be common in their cases.

The question then arose as to whether thyroidectomy resulted in the risk of progressive exophthalmos that the above figures seemed to suggest, or whether the striking clinical features of the condition and frequent sequelae of blindness had led ophthalmologists to overstress the danger. It was therefore felt that a large series of patients who had been submitted to thyroidectomy should be reviewed and an attempt made to assess the true frequency of the condition, both in its grosser form and in the milder asymptomatic form.

It was decided to review all the cases of toxic goitre admitted to the Royal Free Hospital under the care of the late Cecil Joll between the years 1940 and 1944 inclusive. These numbered 1,001 and of these 986 cases had been submitted to thyroidectomy. A questionnaire detailing the symptoms and signs of thyrotropic exophthalmos was prepared and sent to the family doctor of those patients who had been operated on. In instances where the patient was known to have moved from the original district or no reply was received from the doctor a questionnaire, necessarily less detailed, was sent to the patient.

Replies were received from 58 per cent. of those to whom the questionnaire was sent. Any statistical analysis is therefore impossible, but at the same time it is thought that the figures are of interest, and perhaps significant.

An analysis of the 1,001 cases reviewed is given herewith in Table I:

TABLE I

(i) Number of female patients who replied ...	487
(ii) Number of male patients who replied ...	46
(iii) Number of patients who died after operation	36
(iv) Number of patients who could not be traced ...	105
(v) Number of patients who did not reply ...	312
(vi) Miscellaneous	15
Total ...	1,001

Referring to Table I above, it is to be noted that 36 patients have died since operation. In 27 of these cases the cause of death was ascertained, and in no case was there any suggestion of thyrotropic exophthalmos before or at the time of death. Pneumonia was a frequent cause of death of those patients who died soon after operation, while later deaths were often due to carcinoma. Excluding the groups (iii), (iv), (v), and (vi), it is found that only 533 cases are left for consideration for the final analysis.

Each case history was then taken and considered in the light of the pre-operative findings and the reply to the questionnaire for evidence suggestive of thyrotropic exophthalmos. As a result of this 49 patients were asked to report to Moorfields Eye Hospital for further detailed investigation. Twenty patients did not report and ultimately 29 patients were examined. Of these, 9 showed no evidence of any disease whatever, and of the remaining 20, 5 patients showed evidence of hyperthyroidism and 8 were slightly or mildly myxoedematous and were controlled by thyroid extract. One patient suffered from post-operative tetany and one was being treated with stilboestrol for pruritis vulvae. Others showed a variety of minor complaints. Only three patients showed slight evidence of thyrotropic exophthalmos and their case histories are summarised below :—

Case 1. Mrs. S. G., aged 24 years, had a partial thyroidectomy for Graves' disease in 1941. When seen at Moorfields in 1947 she was myxoedematous and complained that her eyes were becoming more prominent. Her eyes were proptosed and the lids oedematous. She appeared to be a definite example of post thyroidectomy thyrotropic exophthalmos.

Case 2. Mrs. C. C., aged 58 years, had a partial thyroidectomy for Graves' disease in June, 1941. Subsequently she became myxoedematous and was given thyroid extract, which she later discontinued. When seen at Moorfields in November, 1947, she had the typical features of myxoedema together with chemosis and proptosis. In this case the myxoedema was complicated by excess pituitary thyrotropic hormone.

Case 3. Mrs. A. B., aged 39 years, became mildly myxoedematous following a partial thyroidectomy in 1944. On examination at Moorfields in addition to slight exophthalmos she showed some puffiness of the upper lids. She appeared to be a mild case of myxoedema with some excess thyrotropic hormone.

The diagnosis of thyrotropic exophthalmos is suggested by the presence of exophthalmos, swelling of the lid due to increasing fat and later stasis oedema, oedema of the conjunctiva and orbital contents and weakness of the extra-ocular muscles. The greatest difficulty in diagnosing mild cases is that there is no readily available means of assessing the thyrotropic hormone content of the blood, and biopsy of the orbital contents is usually not feasible. Therefore the diagnosis and the differential diagnosis of thyrotropic exophthalmos must be purely clinical. However, these cases showed definite evidence of mild thyrotropic exophthalmos, and slight myxoedema. The exophthalmos was slight and none

showed any evidence of diplopia or other disturbance of ocular function. In no case was there any evidence of venous congestion of the retinal vessels or oedema of the disc, nor any gross oedema of the eyelids, nor gross chemosis.

The ages of the patients were evenly spread from late youth to early old age whereas thyrotropic exophthalmos is largely a disease of late middle life. Further, they were all females and the condition is known to be 36 times more common in males than females (Mann, 1948). All three had had seven-eighths of the thyroid removed.

DISCUSSION

The most surprising feature made evident by this investigation is the infrequency of thyrotropic exophthalmos as a sequel to thyroidectomy. The figures of Mann (1946), and others quoted above had suggested that the incidence would be certainly appreciable. It was therefore expected that the review of such a relatively large number of cases in which thyroidectomy had been performed would have revealed a few gross cases and several minor cases of thyrotropic exophthalmos. Gross cases of the condition, owing to their striking clinical features, would obviously have required hospitalisation and would be unlikely to have escaped notice. Nothing suggestive of this type of case was found in the replies received either from the patients themselves, their family doctor or in the notes on the cause of death of patients who had died since operation. Since in all, only three mild cases were discovered the incidence after thyroidectomy appears to be only a fraction of one per cent. Part of this incidence must be attributed to the care in the selection of cases for operation and the technical skill of a surgeon of great experience, the late Cecil Joll. These findings are confirmed in a personal communication from Sir Thomas Dunhill. In his experience of thyroidectomy extending over forty years he has only encountered two cases of thyrotropic exophthalmos. Each of these had been operated on by another surgeon. Among his own operation cases there were several in which some of the signs were those encountered in exophthalmic ophthalmoplegia and in which tarsorrhaphy was performed because of the extreme exophthalmos with chemosis and ulceration, but in all of these the eyes became normal, except in one patient. In this patient one eye was lost—the other eye became normal. Photographs of each of these patients have been published. (Dunhill, 1930.)

With careful surgery it seems that the risk of post-operative thyrotropic exophthalmos is more apparent than real.

SUMMARY

1. Recent literature suggests that thyrotropic exophthalmos commonly follows thyroidectomy.

2. To investigate the true incidence of this as a complication, a questionnaire was submitted in regard to 1,001 patients admitted to the Royal Free Hospital for thyroidectomy from 1940-1944.

3. Satisfactory information was obtained in 584 cases.

4. Three cases, only, of thyrotropic exophthalmos of a mild degree were found.

5. No gross cases of the condition occurred.

6. The condition is rare as sequel to thyroidectomy.

This study was undertaken at the suggestion of Miss Ida Mann and I am much indebted to her for her help and guidance. I wish also to thank Dr. Elizabeth Everitt, formerly of the Royal Free Hospital, for her abstracts of case histories, and Miss Saunders for help with the clerical aspects. Acknowledgments are also due to the Medical Committee of the Royal Free Hospital for their permission to use the notes of the late Mr. Cecil Joll. The secretarial expenses for this investigation have been met by Moorfields Eye Hospital, who made the necessary allocation of funds from the Royal London Ophthalmic Hospital Research Fund.

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THE GLASS ROD TEST IN GLAUCOMATOUS EYES*

BY

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IN his first paper on the aqueous veins Ascher described the so-called " glass rod phenomenon "[1]. This phenomenon is produced by compressing the recipient vessel just beyond the meeting-point of an aqueous vein and a blood vein. There are two possible results. The aqueous may push away and replace the blood in the recipient vein so that it enters the vein previously filled with

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blood. This is called a *positive glass rod test* or *aqueous influx phenomenon*. Alternatively, blood may flow backwards into the aqueous vein, filling it wholly or in part. This is called a *negative glass rod test* or *blood influx phenomenon*.

In normal eyes Ascher has shown[1, 2] that this test can be positive or negative in different aqueous veins. According to his law of constancy[4], however, the test will always give the same result, positive or negative, when performed on the same aqueous vein even after an interval of years. If more than one aqueous vein is present in the same eye, one may show a positive and the other a negative glass rod test. He has also found that aqueous veins situated on the temporal side of the globe show a positive test more often than those on the nasal side. In his first paper on this subject ([1] p. 32 and [2] p. 1192) Ascher says that the ratio of aqueous veins with a positive glass rod test to those with a negative test is about seven to five. In a later paper ([4] p. 1084) he has found statistically that the glass rod test is positive only in two-fifths of all eyes with aqueous veins.

In eyes suffering from simple glaucoma Ascher has made the remarkable finding[1, 2, 3] that the glass rod test is invariably negative except when the pressure is controlled by either miotics or surgery. Goldmann[8] has confirmed this and so does de Vries[12]. The latter has, however, found that the test can be positive even if the ocular pressure is increased, provided the intra-ocular pressure is in the decreasing phase.

Clinical Investigations.

Twenty-four patients with 35 eyes suffering from simple glaucoma and with an aqueous vein suitable for the glass rod test were examined. The glass rod test was applied to each of these eyes many times. Observations were usually made half-hourly through a large part of the day and in most cases for more than one day, sometimes up to five. As the ocular tension was expected to influence the result of the test, the tension was measured with a Schiötz X-tonometer after each test. Before tonometry a drop of 1 per cent. pantocaine was instilled into the eye. The drops and the manipulations irritated the eye and produced a state of hyperæmia which usually disappeared in half an hour. If the hyperæmia persisted, a further delay in testing was necessary. The eyes examined had not been operated on, and usually not treated with miotics for 24 hours. The tension in most of the eyes oscillated considerably during the period of observation and it could be seen that the result of the test varied with the height of the ocular tension and with the phase of its oscillations.

When the bulbar tension was in an increasing phase the test was never positive. It is, however, often difficult or even impossible to judge the result of the test in this phase as the aqueous veins are usually filled spontaneously with blood. When the bulbar tension was in a decreasing phase de Vries' findings were confirmed in so far as the test was sometimes found to be positive even when the bulbar tension was increased. It was, however, by no means invariably so. In this connection it does not seem to matter whether the decreasing phase is spontaneous or produced by pilocarpine. When the tension remained on a steady but increased level the test was usually negative. In a few cases, however, it was positive in spite of a tension up to 45 mm. Hg.

Ascher's finding that the glass rod test is always negative in glaucomatous eyes when the bulbar tension is increased was thus not confirmed here. The test is definitely more often negative in glaucomatous eyes. Nor was Ascher's law of constancy found to apply to glaucomatous eyes. Repeated examinations of the same aqueous vein very often gave different results. In 21 of the glaucomatous eyes examined, an inconstancy of the glass rod test was found. In one case for instance the glass rod test was applied to the same aqueous vein 14 times, 9 of which were positive and 5 negative. The bulbar tension oscillated between 15 and 25 mm. Hg during the three days' observation. In this case no direct relationship between the height of the tension and the results of the tests could be observed, although it is probable that the phases in the oscillations of tension determined the variations. The bulbar tension went up and down so quickly that it was impossible to be sure whether the test was carried out during an increasing or decreasing phase.

DISCUSSION.

Some hydrodynamic principles of the aqueous veins will first be explained.

According to Theobald[9] there are 20 to 30 outlets from the canal of Schlemm. Most of them join the veins within the sclera, but one or a few may appear on the bulbar surface before they join a blood vein; the latter are known as aqueous veins. The total amount of fluid emptied through all the outlets in a normal eye must be just as much as is necessary to keep the production and escape of aqueous humour in equilibrium. The outlets, however, differ in size, length and course. Both the amount of fluid which has to be emptied through each of them and their pressures at the point where they join the blood vein must therefore vary from one outlet to another. On the other hand, the pressure in the blood

veins is not uniform. Inside the globe the venous pressure is high but it starts decreasing as soon as the vein enters the sclera. The pressure in the vein just at the meeting point with an aqueous outlet vein may therefore vary considerably.

From this, it is clear that the amount of fluid which normally passes through an aqueous vein, will be specific for each individual vein. Both the aqueous vein and the blood vein will discharge their contents into the recipient vein even if their pressures, within certain limits, are unequal. The ratio between the amount of outflow from the two vessels will depend, among other things, on the ratio between their end-pressures. Some aqueous veins will therefore normally have a higher pressure and others a lower pressure than that of the joining blood vein.

When the recipient vein is compressed the flow through the vessels will be stopped for a while and that vessel which now has the higher pressure will push its contents up into the vessel with the lower pressure. If, for instance the pressure in the aqueous vein is the higher, the glass rod test will be positive. In accordance with hydrodynamic laws, however, the pressure in both vessels will change until the pressure at the first branching higher up the stream is attained. In other words, the final new pressures not only depend on the previous pressures at the meeting point but also on the fall of pressure which takes place in the respective vessels from the most proximal branching. Now, this fall of pressure will be different for each aqueous vein and blood vein and will depend among other things on the distance from the proximal branching to the meeting point. This new local factor is thus of importance in determining the result of the test.

These facts readily explain Ascher's findings as to the glass rod test in normal eyes. The local circumstances are indeed so different for each aqueous vein that the test applied to some veins will be positive, and to other veins negative. It also explains his law of constancy.

The findings in glaucomatous eyes are, however, not so easy to understand. Both Goldmann and Ascher have tried to explain why the glass rod test is negative when the bulbar pressure is increased. Goldmann emphasises [8] that it is due to an increased resistance in the permeable membrane between the anterior chamber and Schlemm's canal. This should result in a low pressure in Schlemm's canal and in its outlets, including the aqueous veins; on the other hand it could cause the increased bulbar tension. If, however, the rate of production of aqueous humour is unchanged, the bulbar pressure and therefore the pressure in the aqueous veins will rise until the outflow is the same as before. A constant decreased pressure in the aqueous veins is therefore only

possible if the production of aqueous humour decreases when the bulbar pressure increases. This may or may not be so, but Bárány's findings [7] seem to indicate that production of aqueous humour is independent of the bulbar pressure.

If Goldmann's conception is correct, the following three facts would suggest that the resistance in the permeable membrane alters very often and quickly and at times is even less than normal.

1. The occurrence of large oscillations in the bulbar tension which usually take place in glaucomatous eyes.
2. The extraordinarily great outflow of clear liquid seen when the bulbar pressure is in a decreasing phase [11].
3. The fact that the glass rod test does not show the same constancy as in normal eyes.

It follows then, that Goldmann's theory can only be accepted if a rapid alteration in the resistance of the permeable membrane can take place and if the production of aqueous humour decreases when the ocular pressure increases. The first of these conditions is improbable and the second doubtful.

Ascher has also explained the negative glass rod test by postulating a decreased pressure in the aqueous veins[4, 5, 6]. He finds it more likely, however, that the hampering of the outflow is caused by a narrowing of the outlets from Schlemm's canal. It is perhaps more credible that such a narrowing may be reversible but Ascher's explanation, like Goldmann's, is entirely dependent on a decreased production of aqueous humour when the bulbar pressure is increased.

The aqueous veins are usually, as Goldmann emphasises[8] direct branches from Schlemm's canal. This is, however, not always the case. When they are direct branches it is impossible that their constriction can cause a negative glass rod test. Such a narrowing would cause an unusually high pressure in the canal of Schlemm and as the glass rod test depends on the pressure at the first branching higher up the stream, the test would tend to be more positive than ever.

In my opinion the cause of the phenomena appearing in glaucomatous eyes must be sought not in the aqueous veins, but in the blood veins. Ascher has also mentioned this possibility [3] but he has not followed it up.

There are two circumstances concerning the venous pressure that will play a part in the determination of the direction of flow. The higher the bulbar pressure, the higher must be the intrabulbar venous pressure. On the other hand, the general venous pressure in the orbit will be the same. The pressure gradient in the veins when they pass through the sclera and along the epi-

sclera must therefore be steeper if the bulbar pressure is high. The fall of pressure from the proximal branching to the point of meeting with an aqueous vein must therefore also be greater, thus tending to cause a negative glass rod test. On the other hand, it has been shown[10] that the venous pressure is high in proportion to the bulbar pressure when the latter is in an increasing phase. This fact also tends to cause a negative glass rod test. When the bulbar pressure is in a decreasing phase, however, the venous pressure is low compared with the bulbar pressure and thus tends to make the test positive. The combination of these facts can explain the irregular findings with the glass rod test in glaucomatous eyes. One has, however, also to take into account the fact that the result of the test is normally vigorous in some veins while in others it is feeble. The fact that it must be easier to change a feeble test than a vigorous one probably explains why the test is sometimes positive even when the bulbar tension is increased and why, in other eyes, the result of the test frequently changes in response to minor oscillation in the tension.

SUMMARY

The glass rod test was applied to 35 eyes suffering from simple glaucoma.

When the bulbar tension was increased the test was usually found to be negative. It was, however, found to be positive when the ocular tension was in a decreasing phase and sometimes when it was on a steady, but increased level. The most striking difference between normal and glaucomatous eyes is that Ascher's law of constancy does not apply to glaucomatous eyes. Early investigators' explanations as to the cause of the negative glass rod test in glaucomatous eyes are discussed. The author emphasises that the state of the venous pressure provides the most rational explanation of the findings.

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EXTRACTION OF CATARACT IN A CASE OF SYMPATHETIC OPHTHALMIA*

BY

F. W. G. SMITH

MARGATE

THE summary in Ophthalmic Literature of an article by A. Franceschetti[1] has prompted me to report this case.

In October, 1946, Mrs. A., aged 79 years, with bilateral cataracts, underwent a left extra-capsular extraction without any obvious operative complications, but two days after operation an acute iridocyclitis developed. The usual treatment was undertaken, and both eyes observed carefully with the slit-lamp. Enucleation was advised after five weeks, as the left eye had a marked flare, many plastic keratic precipitates and new vessels in the iris. The tension was low, and she had recurrent attacks of ciliary pain.

The day after the left eye was enucleated tvpical sympathetic ophthalmia developed in the right eye, which, after much treatment and many distressing symptoms, settled down, but showed a slight flare, many K.P., posterior synechiae, and the pupil occluded by exudate. The tension became low. By mistake a section of the enucleated eye was not carried out, but clinically all the signs of sympathetic ophthalmia were present. The case had been examined several times with the slit-lamp before operation, and there had been no evidence of previous iritis.

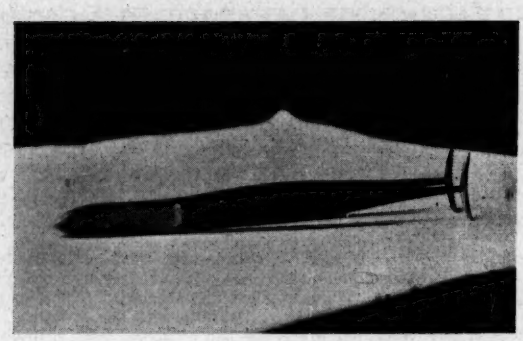
As the projection of light was good in the remaining eye it was felt that some risk might be taken owing to the age of the patient. Nineteen months after the onset of the disease, extraction was undertaken with the usual akinesia, retrobulbar anaesthesia, bridle suture and, in this case, a Stallard's corneal suture. A large corneal section was made, and retraction of the cornea by the suture allowed the excision of a large portion of iris and capsule with a capsule forceps. The lens was lifted out, without vitreous loss, by two Ziegler needles inserted into its substance. 20,000 units of white penicillin in 1 c.c. *aq. dest.* were dropped on the eye before, during and after operation. The removal of the lens was easier than in the case described by J. Herbert Fisher,[2] where the cataract was extracted seven years after the onset of the disease.

The eye settled down quickly, and one month later an opening was made with a fine Graefe knife in the thick but soft membrane remaining. The corrected vision was reduced to 3/60 on account of a white plaque in the macular area, which might have been the result of a coalescence of Dalen's spots, but the peripheral field was full, and the patient was able to get about and undertake household work.

I have found the above method of extraction useful in complicated cataract with many iris adhesions. One Ziegler needle with slight external pressure on the lower pole, or two needles without external pressure, can be helpful in extracting the lens, and also when the capsule has burst in an intra-capsular extraction. A fine straight, non-toothed iris forceps instead of a corneal suture retracts the cornea. I have ceased to use the latter in routine cataract extractions.

The fixation forceps in the illustration are a type used by Dr. Frank Burch (Senior) of St. Paul, Minnesota, and they have many practical advantages. Their 20 into 19 teeth provide excellent fixation, whether the conjunctiva is normal, friable or oedematous,

* Received for publication, April 4, 1949.



Conjunctival Fixation Forceps.

and the breadth of grip helps to prevent rotation of the eyeball in a Graefe section if the knife is not quite perfect.

It is suggested that, where cataract has developed in cases of sympathetic ophthalmia, fairly early operation might be undertaken when the slit-lamp does not show undue inflammation and the acute recurrences have subsided, despite the presence of keratic precipitates and a slight flare. The irido-capsular membrane may be softer and an opening made more easily to lift out the lens. The same would seem to apply to the after-cataract.

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SIMPLE CAMERA SUPPORT FOR THE OPERATING THEATRE

BY

GY. P. HALBERG, M.D.

ARGENTINA

THE usual photographic tripods are often inconvenient and cumbersome when used in the theatre for the photography of eye operations. For this reason a simple *unipod support* has recently been designed. A short illustrated specification is given below.

The unipod consists of a vertical iron rod, and a horizontal flat iron tongue, supported at 90° by a simple diagonal bar. The vertical member is ½ in. solid rod, 36 in. in length. The horizontal portion is flat; 24 in. long, 1¼ in. wide and ¼ in. thick. Two slots

10 in. × ¼ in. are made in its long axis to facilitate the adjustable fixing of a ball and socket camera support (Fig. 1).

The whole assembly is fixed to the operating table as shewn in Fig. 2.

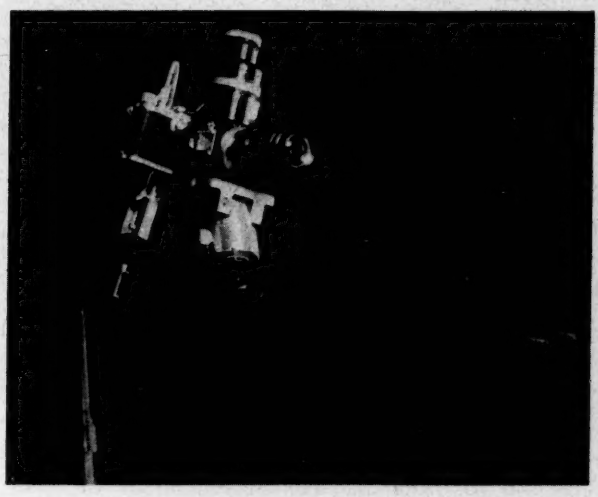


FIG. 1.

Unipod camera support, with camera and "ball and socket joint."

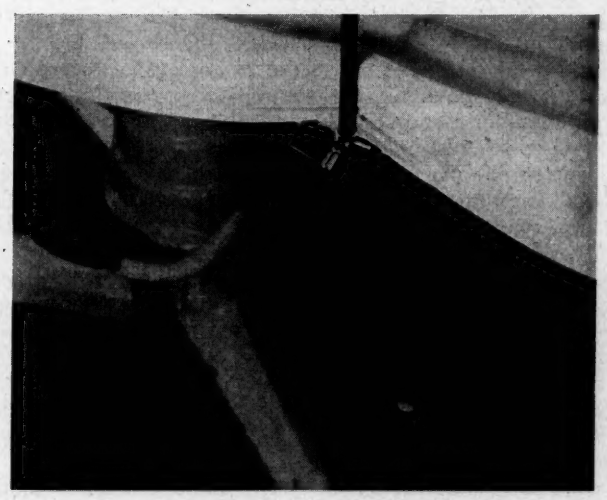


FIG. 2.

Picture shows how unipod support is fixed to the operating table.

OPHTHALMOLOGY IN AUSTRALIA

THE Ninth Annual Congress of the Ophthalmological Society of Australia (B.M.A.) was held at B.M.A. Hall in Melbourne from October 3 to 7 under the presidency of Dr. Arthur Joyce. Abstracts of the papers will in due course appear in Ophthalmic Literature, but meanwhile the organisers of the Congress are to be congratulated upon their achievement. Dr. A. L. Lance (Sydney), the Honorary Secretary of the Society, had collaborated so efficiently with the local Honorary Secretaries of the Congress, Dr. Esmé Anderson and Dr. S. R. Gerstman of Melbourne, that all the arrangements worked smoothly, and success was finally clinched by the atmosphere of free, informal discussion communicated by the President.

At the opening session members were gratified to hear a message of greeting from Sir John Parsons, a confirmed admirer of Australian scientific talent. Among the contributors to the scientific programme were Dr. Ronald Lowe (Melbourne) and Dr. Hugh Ryan (Melbourne), whose energetic work at the Institute of Ophthalmology and elsewhere in London is fresh in the memory of English ophthalmologists. Another junior ophthalmologist, Dr. K. B. Redmond (Orange), gave a carefully prepared paper on the causation and prevention of blindness. Dr. Kevin O'Day's (Melbourne) discourse on iris tumours was illustrated by excellent micro-photographs, and Dr. J. Ringland Anderson (Melbourne) was as stimulating as ever. There were also interesting communications from Dr. J. Bruce Hamilton (Hobart), Dr. Norman Macindoe (Sydney), Dr. G. A. Brew (Melbourne), Dr. J. L. R. Carter (Launceston) and Dr. D. T. Shortridge (Warrawee).

Miss Ida Mann spoke about the movement of macrophages in corneal grafts. She also gave an illustrated account of the Institute of Ophthalmology in London, and showed a film recording her former visit to Australia. A paper in which Mr. Frank Law, President of the Faculty of Ophthalmologists, had recorded his unofficial impressions about ophthalmology under the National Health Service was read out by Mr. J. H. Doggart. Mr. Doggart and Mr. T. Keith Lyle each gave two other talks. One of the afternoons was devoted to a clinical meeting at the Eye and Ear Hospital, where a rich array of material had been assembled. Discussion of the cases followed under the chairmanship of Dr. Walter Gibson (Brisbane). Honorary membership of the Society was conferred upon Mr. J. H. Doggart and Mr. T. Keith Lyle, who expressed to the President their warm appreciation of this honour. It will be recalled that Miss Ida Mann was similarly honoured on the occasion of her previous visit to Australia.

The present writer retains vivid memories of hospitality generously

dispensed by the President and Mrs. Arthur Joyce, Dr. and Mrs. J. Ringland Anderson, Dr. and Mrs. W. Box, Dr. and Mrs. Kevin O'Day, Dr. and Mrs. Mark Gardner, Dr. Esmé Anderson and many others, including the Council of the Australasian College of Surgeons. He will never forget also the expedition to Warrandyte, where Dr. and Mrs. Edward Gault entertained a number of congressists shepherded by his daughter and colleague, Dr. Adelaide Gault. Although Dr. Edward Gault is well into the ninth decade of life, he stood up as straight as a lance, to make his speech at the Annual Dinner. It was at this same banquet that Dr. Archie Anderson (Melbourne) made his memorable *mot:* "Ida came out to us ten years ago, every inch a Mann; and now she's come back a regular Gye."

A medical man who spent several years in Australia described its people as the most hospitable in the world. Certainly nothing could have been kinder than the welcome accorded to the guest speakers from England. Nothing was left undone to promote their enjoyment and to put them at ease in this glorious city, and so the memory of their visit to Melbourne is exceedingly precious—and all the more so, by reason of the enthusiasm with which the coming generation is attacking ophthalmological problems on the continent of Australia.

TASMANIA

On October 12 a meeting of the Tasmanian Section of the Ophthalmological Society of Australia was held at the Royal Society's room in the Tasmanian museum at Hobart. Mr. J. H. Doggart spoke on retinopathy in the diabetic, and Mr. T. Keith Lyle's subject was traumatic surgery of the face. The chair was occupied by Dr. J. Bruce Hamilton, to whom these visitors are deeply indebted for a multitude of reasons. Not only were they hospitably entertained in the home of Dr. and Mrs. Bruce Hamilton, but they were also shown the apple-blossom of the Huon riverside and introduced to a multitude of other delightful friends, including Dr. and Mrs. Alec Budge, who met them on arrival at Wynyard and made them so welcome at Devonport. Dr. and Mrs. Tim Palfreyman were also in the vanguard of those who loaded us with kindness, and other delightful hosts were Dr. and Mrs. J. L. R. Carter, Dr. and Mrs. D. H. Waterworth, Dr. T. G. H. Hogg (a nephew of Mr. Rupert Scott) and Dr. J. L. Grove. Hobart and Launceston seem to be full of warm-hearted people, and Tasmania might well be described as a series of enchanting landscapes.

NEW ZEALAND

The Annual Congress of the Ophthalmological Society of New Zealand took place last May, but a special conference, to which the visiting speakers at the Australian Congress were invited, was held

at Christchurch on October 26 and 27. Miss Ida Mann was unable to attend, though she hopes to re-visit New Zealand in the near future. The President of this gathering was Dr. W. H. Simpson (Wellington), a former Moorfields House Surgeon, whose son, now settled in Vancouver, recently occupied the same post. Dr. Simpson is remarkable for his lively wit and geniality of presence, so that the success of the meeting was virtually certain from the outset. Dr. W. J. Hope-Robertson (Wellington), the Honorary Secretary-Treasurer of this young and vigorous Society, is to be congratulated upon his organising zeal, and great credit is also due to Dr. Harry Wales, the local Honorary Secretary, and to Dr. Lindsay Burns, also of Christchurch. The wives of these four ophthalmologists all played a prominent part in the social side of the meeting.

Mr. J. H. Doggart and Mr. T. Keith Lyle each contributed three papers, and an interesting group of clinical cases was discussed under the chairmanship of Dr. Lindsay Burns, a former Moorfields House Surgeon. A fascinating talk on artificial eyes in ancient Egypt was given by Dr. Rowland Wilson, whose distinguished work at the Giza Memorial Laboratory is known throughout the world of ophthalmology. The width of Dr. Wilson's clinical and scientific interest is remarkable, so that he is able to make stimulating queries and fruitful suggestions about almost every conceivable subject. Certainly he exerted a strong fertilising influence during the discussions which followed the papers.

Before the Christchurch meetings, Mr. Doggart and Mr. Lyle were entertained by the Auckland ophthalmologists at a dinner over which Dr. W. A. Fairclough presided. Dr. H. V. Coverdale, Dr. Graeme Talbot, Dr. Calvin Ring and a number of other old friends were present at what proved to be a most successful evening's entertainment. Here and elsewhere in New Zealand it was a special joy to see former colleagues and house surgeons happily settled, and carrying on with the excellent work which we had learned to expect from them by reason of their former activities in Great Britain. Mr. Lyle snatched a few days away from the preparation of his discourses, and took Mrs. Lyle to browse on the beaches of North Island, and to career over the roads in a car lent by his former house surgeon, Dr. Charles Swanston. Mr. Doggart was generously welcomed at Dunedin by Sir Charles Hercus, the Dean of the Medical School of Otago University, and gave a talk to the students. He was hospitably entertained by Dr. and Mrs. Rowland Wilson, and was also enabled by Dr. Wilson to see something of the work of that enterprising cranio-surgeon, Dr. Murray Falconer. Mr. Doggart also visited Dr. Ryburn at Knox House, under the wing of Dr. John Stewart, and afterwards the latter's father, Dr. Garfield Stewart (Auckland), conducted Mr. Doggart to Queenstown, where

he watched the sun rise over Lake Wakatipu, and revelled in the splendour of Milford Sound. Dr. and Mrs. John Doctor regaled the visitors at their charming Waikanae home, and Mrs. Garfield Stewart once again proved herself to be a wonderful hostess in Auckland.

New Zealand is a land of infinite variety, and it is curious to think how few miles intervene between the austere peaks of the Southern Alps, and the lambs that frolic over the Canterbury plains. Christchurch, whose winding river and green grass recall the quietude of Cambridge and Salisbury, conveys an atmosphere altogether different from that of Dunedin, Wellington and Auckland, but one feature is common to all the cities of New Zealand—a kindly welcome to friends from across the sea.

ADELAIDE AND SYDNEY

Miss Mann and her husband, Professor W. E. Gye, called at Adelaide during their sea voyage to Melbourne, and were welcomed by Dr. and Mrs. A. L. Tostevin, who also lavished hospitality on Mr. Doggart before the Melbourne conference. Mr. Doggart visited the Adelaide Children's Hospital under the guidance of Dr. Geoffrey Barham Black and Dr. D. O. Crompton. On October 14 a number of interesting cases were discussed at a clinical meeting preceded by a dinner to which Dr. Tostevin had bidden his Adelaide colleagues and his visitor. To the writer of this article it was a memorable experience to bestride the Oval cricket ground, to sail across the inner harbour, and to hear the twanging of innumerable frogs intermingled with the kookaburra bird's chatter. The inhabitants of Adelaide have good reason to revere the memory of Colonel Light, whose forethought and determination are mirrored in the lay-out of this lovely city.

Mr. and Mrs. T. Keith Lyle, who travelled *via* Vancouver, reached Sydney on September 25 and were followed two days later by Mr. J. H. Doggart. They spent a few days there before the Melbourne meetings, another day or two before going to New Zealand, and again nearly a week before the final departure on November 4. With Dr. V. M. Coppleson in the chair, the New South Wales representatives of the Royal Australasian College of Surgeons generously entertained Mr. Doggart and Mr. Lyle to dinner at the Australian Club on October 31, and afterwards the visitors each contributed a paper in the lecture hall of the College of Physicians. Dr. Stephen Lynch, who formerly worked at King's College Hospital with Mr. H. Willoughby Lyle, crowned the evening with a rousing welcome by Mrs. Lynch and himself at their beautiful Vaucluse home.

Mr. Lyle also addressed the New South Wales Ophthalmological

Society on November 2—a meeting which Mr. Doggart was unable to attend, because he was basking in the hospitality of Dr. and Mrs. Clifford Colvin at Orange. One of Mr. Doggart's most stimulating experiences was a visit to Dr. Mervyn Archdall at the editorial headquarters of the Medical Journal of Australia. It is seldom realised in England that Printing House, Seamer Street, not only produces that magnificent Journal, but also issues an abundant jet of other periodicals, text-books, works of reference, etc. It was a great privilege to meet the manager, Mr. Noldt, and many other members of Dr. Archdall's happy team of colleagues. This beloved editor was one of the most popular figures at the Melbourne congress, and he was also a guest at Dr. and Mrs. Bruce Hamilton's Hobart party on October 13. The evening which Mr. Doggart spent with Dr. and Mrs. Archdall at their home on November 3 stands out as a treasured memory.

It was a joy to renew friendships with Dr. E. A. Brearley, Dr. W. M. C. MacDonald and Dr. Norman McA. Gregg. Dr. Gregg returned from his world trip shortly after the Melbourne meetings, leaving his wife and family for a further stay in England. It will be recalled that he was a particularly welcome overseas visitor at the B.M.A. Harrogate Meeting this summer. Dr. and Mrs. Darcy Williams were the very personification of kindness, and the writer is for ever indebted to them for bountiful help and attention. Both Mr. Doggart and Mr. Lyle found time to visit the building of the Medical Eye Service, where consultations at reduced fee are available on the clinic system. Dr. Darcy Williams' enterprise was largely responsible for the inauguration of this venture, which has proved a great boon to patients of moderate means.

Other friends to whose kindly welcome and generous hospitality in this thrilling city the writer would like to pay tribute are Dr. and Mrs. Cedric Cohen, who may rest assured of a warm welcome at the forthcoming International Congress, the Honourable and Mrs. Arthur Colvin, Dr. and Mrs. Clifford Colvin, Dr. and Mrs. Arnold Lance, Mrs. Claffy and her son Frank (a former house surgeon at the Central London Ophthalmic Hospital), and Father Frank Flynn, who loomed up in the dawn at Port Darwin with the same endearing smile as of old.

For every name that has been mentioned there are several times as many who contributed to the warmth of our welcome. Every invitation accepted was only one of a number which the swift passage of time rendered impossible of acceptance. Therefore many hospitable people worthy of mention must perforce be omitted, but they may rest assured that their generosity did not pass unnoticed. We who have been privileged to work as colleagues in peace and in war with men who came from all parts of Australasia felt certain that it would be a joy to enter their homes, and a

source of stimulation to take a share in their professional conferences: but the event exceeded all expectations, so that we are profoundly indebted to the good folk of Australia, Tasmania and New Zealand; and we are fortified in the conviction that we should mingle more closely with each other. Let fresh links be forged, and that right early.

BOOK NOTICE

Ophthalmic Medicine. By JAMES HAMILTON DOGGART. Twenty-eight coloured plates, 87 text figures. J. and A. Churchill, Ltd. 1949. Price, 32/-.

Only a select few in this country have attempted the difficult task of writing a text-book on the medical aspects of ophthalmology. In the wake of the late Sir William Gowers and Foster Moore comes J. H. Doggart with this admirable book on " Ophthalmic Medicine " succeeding by 24 years Foster Moore's second edition of Medical Ophthalmology, published in 1925. The qualities necessary to do full justice to this subject are considerable. The author of " Ophthalmic Medicine " has brought to this work the stored riches of his extensive clinical experience, a wide knowledge of his specialty and of its many contacts with the main body of medicine, the application of his philosophic mind to controversial matters, and an ease of expression in good English which makes the reader enjoy the book as an absorbing narrative. It is touched and enlightened here and there with advice which shows clearly the author's insight into the art, apart from the technique, of practising medicine. The book has achieved the author's purpose in its presentation of a comprehensive survey of the disorders and diseases of the eye in association with pathological changes in its adjacent structures and in remote parts of the body. In this work he has correlated recent discoveries with the traditional aspects of medical ophthalmology.

The physician will be much helped by four well-written chapters on the history of a case, symptoms, methods of examination and physical signs, and the ophthalmologist by the admirable dissertations on allergy; vitamin defects; inflammatory syndromes; focal, virus and fungus infections; metabolic disorders; and disturbances in endocrine function among other topics of general medical interest.

This book is a praiseworthy attempt to compress into 300 pages all that is sound in the teaching of ophthalmic medicine. It is well illustrated, and a fair bibliography is given at the end of every chapter. There is little to criticise adversely. It is evident that a mistake has been made in Plate XX, Fig. 2, where a tigroid

fundus is printed instead of that of an albino. Plate I, Figs. 1 and 2 could be more artistically executed, and this also applies to the drawings of a pterygium and a dermolipoma of the bulbar conjunctiva.

The book is well produced, and will be valued by physicians and ophthalmologists as a sound contribution to matters concerning both.

NOTES

Death

AS we go to press we learn with deep regret of the death of Sir Herbert Lightfoot Eason, C.B., C.M.G., President of the General Medical Council. An Obituary Notice will be published in the next number of the Journal.

* * * *

Honours

AT their meeting in Chicago in October, 1949, the American Academy of Ophthalmology and Otolaryngology conferred an Honorary Fellowship and an Award of Merit upon Sir Stewart Duke-Elder, who was their "Guest of Honour" at this meeting. During the following week he also received the Honorary Fellowship of the American College of Surgeons.

* * * *

The American Ophthalmological Society

THE American Ophthalmological Society elected new officers at its recent meeting at Hot Springs, Virginia:—*President*, Dr. Parker Heath, Boston; *Vice-President*, Dr. John H. Dunnington, New York; *Secretary-Treasurer*, Dr. Maynard C. Wheeler, New York.

The 1949 Transactions of the American Ophthalmological Society published in book form may be purchased by advance subscription. This volume contains the scientific papers given at the Annual Meeting, and the thesis for membership. Price $12.00. Order from the Editor: Dr. Wilfred E. Fry, 1930 Chestnut Street, Philadelphia, Pa. Orders must be in by December 1.

* * * *

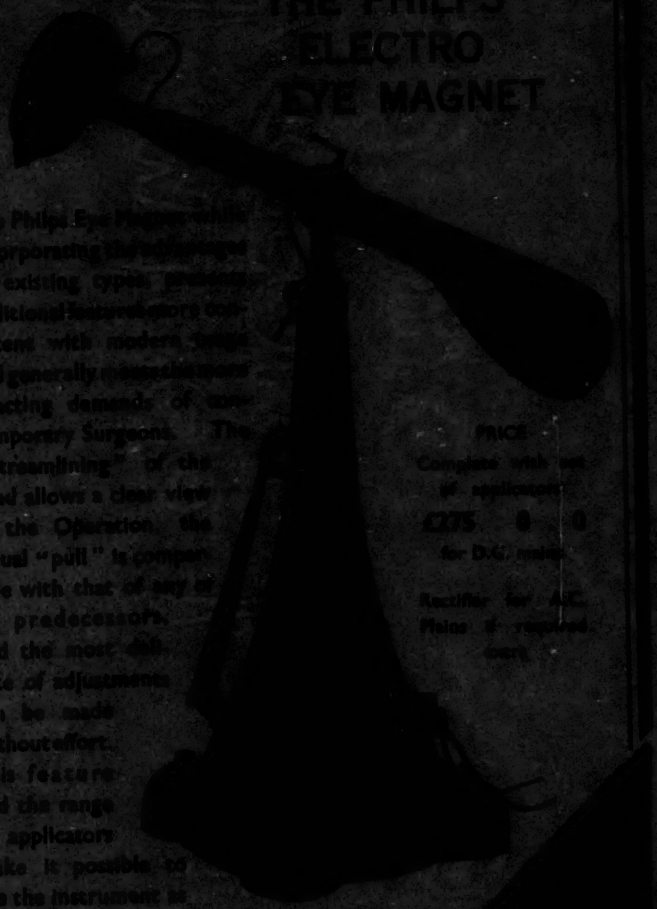
National Society (U.S.A.) for Prevention of Blindness

THE next annual conference of the National Society (U.S.A.) for the Prevention of Blindness will be a combined meeting with the Pan-American Association of Ophthalmology, and will be held March 26 to 30, 1950, at the Hotel Floridian, Miami Beach, Florida.

Among the topics to be discussed at the conference are current blindness prevention programmes in the countries of the Western Hemisphere, trachoma, industrial ophthalmology, eye problems of school children, medical and social management of the glaucomas.

The conference is open to all interested persons, and the Executive Director is Franklin M. Foote, M.D., National Society for the Prevention of Blindness, 1790 Broadway, New York 19, N.Y.

THE PHILPS ELECTRO EYE MAGNET



The Philps Eye Magnet while incorporating the advantages of existing types presents additional features which are consistent with modern design and generally re-establishes exacting demands of contemporary Surgeons. The "streamlining" of the head allows a clear view of the Operation, the actual "pull" is comparable with that of any of its predecessors and the most delicate of adjustments can be made without effort. This feature and the range of applicators make it possible to use the instrument as both a "giant" and hand magnet.

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